DISSERTATION ON

HISTOPATHOLOGICAL STUDY OF ENDOMETRIAL CURETTINGS IN WOMEN WITH ABNORMAL UTERINE BLEEDING AND IMMUNOHISTOCHEMICAL STUDY OF ESTROGEN AND PROGESTERONE RECEPTOR EXPRESSION IN PERIMENOPAUSAL AGE GROUP

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment of the requirement

for the award of degree of

MD BRANCH – III

PATHOLOGY

KARPAGA VINAYAGA INSTITUTE OF MEDICAL SCIENCES,

MADURANTAGAM.

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,

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CERTIFICATE

Certified that this dissertation entitled **"Histopathological Study of Endometrial Curettings in Women with Abnormal Uterine Bleeding and Immunohistochemical Study of Estrogen and Progesterone Receptor Expression in Perimenopausal Age Group"** is a bona fide work done by **Dr. S. Manjani,** Post graduate student, Karpaga Vinayaga Institute of Medical Sciences, Madurantagam, during the academic year 2013 – 2016.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"Histopathological Study of Endometrial Curettings in Women with Abnormal Uterine Bleeding and Immunohistochemical Study of Estrogen and Progesterone Receptor Expression in Perimenopausal Age Group"** submitted by me for the Degree of M.D is the record work carried out by me during the period from August 2013 to September 2015 under the guidance of Dr. T. Chitra, Professor and Head of Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and has not formed the basis of any degree, diploma or fellowship titles in this or any other University or other similar Institution of Higher learning.

Place: Dr. S. Manjani,

Date: Post-graduate student in Pathology.

Signature of the guide

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ACKNOWLEDGEMENT

I sincerely thank DR. R. ANNAMALAI, Managing Director, Karpaga Vinayaga Institute of Medical Sciences for his kindness in helping us with all available resources.

I wish to thank DR. A.R. CHAKRAVARTHY, Dean Karpaga Vinayaga Institute of Medical Sciences for his support and guidance.

It is beyond words to express my sincere thanks and gratitude to my teacher and guide DR. T. CHITRA, professor and Head of Department of pathology, KIMS who consistently guided me in each and every step of my thesis work. Her kind support and encouraging words are great pillars of my success.

I wish to proudly thank my teacher and professor DR. A.B. HARKE for his valuable advice and support.

I feel happy to thank DR. E. SARAVANAN, Associate professor for his guidance and support rendered all through my work.

It also gives immense pleasure in thanking DR. S. KARTHIK, DR. B.SHOBANA AND DR. R. VIMAL assistant professors, for helping me in overcoming difficult situations during this thesis work and for their valuable guidelines.

I also thank my technical staffs Mrs. Daisy, Mrs.Jayanthi, Miss Darwin and nontechnical staffs of department of pathology for their excellent laboratory work.

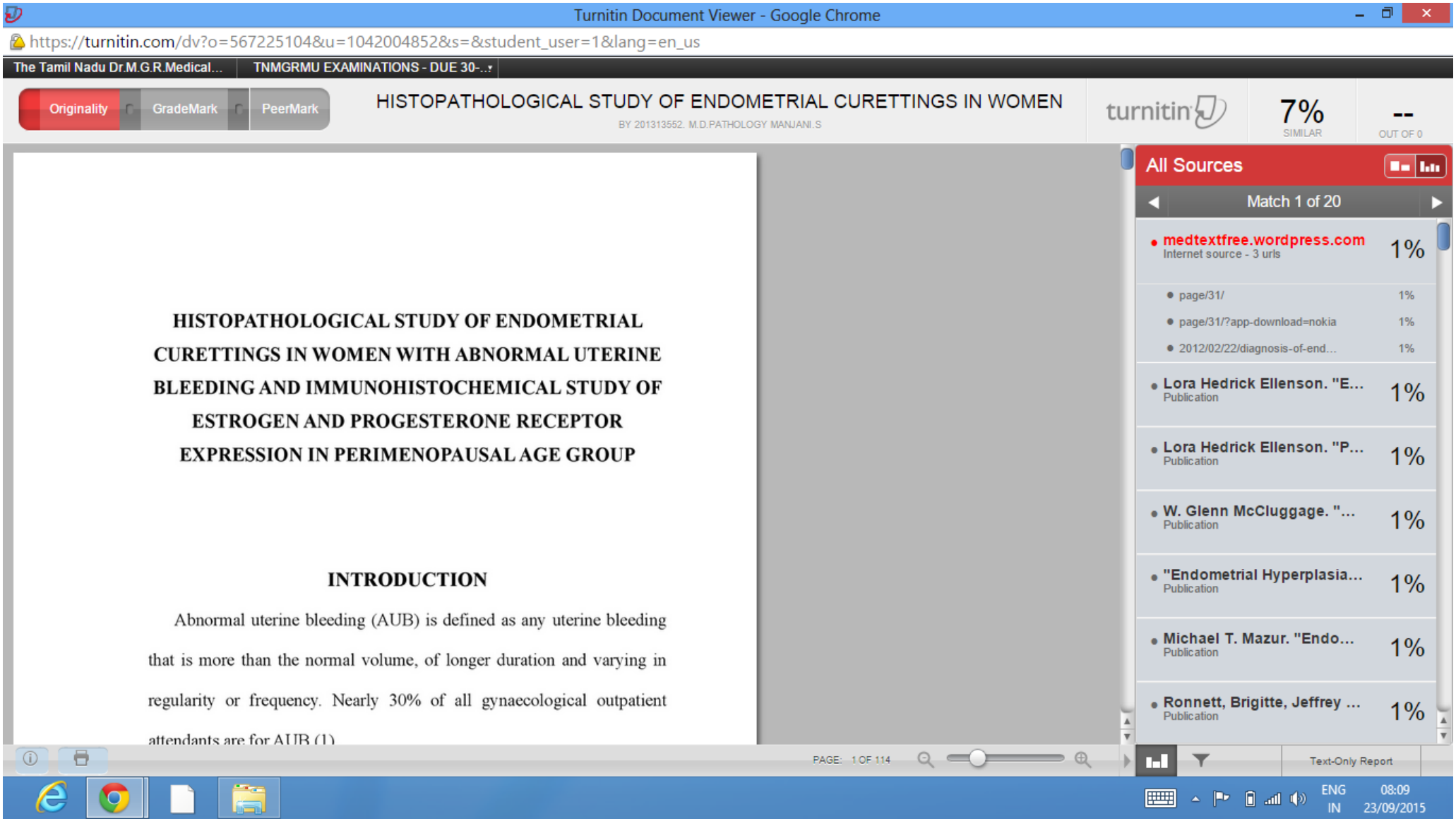
I also take pleasure in thanking the department of Obstetrics and Gynaecology for their help and support throughout the period of study.

I lovably thank my parents for their support and encouragement.

My completion of thesis would have not been accomplished without the support of my husband Dr. C.S. Arulparithi and my daughter, who were always pillars of strength in all my endeavours.

Finally I thank my postgraduate colleague and my junior colleagues for their support.

Above all I thank almighty for his blessings.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INTRODUCTION
Abnormal uterine bleeding (AUB) is defined as any uterine bleeding that is more than the normal volume, of longer duration and varying in regularity or frequency. Nearly 30% of all gynaecological outpatient attendants are for AUB (1)
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INTRODUCTION

INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as any uterine bleeding that is more than the normal volume, of longer duration and varying in regularity or frequency. Nearly 30% of all gynaecological outpatient attendants are for AUB (1).

Abnormal uterine bleeding (AUB) is a collective terminology that includes both organic and non-organic causes. Dysfunctional uterine bleeding (DUB) is a subgroup of AUB that includes abnormal bleeding due to non-organic causes. It is present in 50% of the women with AUB. An endometrial biopsy is usually done for abnormal uterine bleeding to rule out organic pathology. Age and menstrual history are particularly important, because the etiologies of abnormal uterine bleeding differ according to the age and menstrual status (2). In women of reproductive age group, pregnancy complications, including abortion are more common, whereas in postmenopausal women atrophy and organic pathologies are common (3).

A diagnosis of Dysfunctional uterine bleeding can only be made after the histopathological examination has ruled out organic causes (4). Three patterns are commonly seen in DUB. The first is called as “estrogen breakthrough bleeding”, which occurs in the presence of continuous estrogen production by a “persistent follicle”. The proliferated endometrium increase in size so that it outgrows its own blood supply and breakthrough bleeding ensues. The second one is called “estrogen withdrawl bleeding” which is due to “failed follicle”, i.e.

the follicle produces subnormal estrogen. Both these causes are attributed to anovulation. The third finding is “ovulatory endometrium” due to follicular or luteal phase defects.

The cyclical release of estrogen and progesterone from the ovaries control the normal cyclical physiological changes that occur in the endometrium of women during the reproductive period (5). The concentration of receptors for these hormones also vary cyclically during the menstrual cycle. Estrogen and progesterone receptors are also expressed in hyperplasias and endometrial cancers, especially type I. These receptor levels can give important prognostic information. They also give information about the amenability to hormonal therapy.

Hormonal imbalance is the main factor involved in the pathogenesis of Dysfunctional Uterine Bleeding. This alteration is better studied by a combination of histopathological and immunohistochemical evaluation of the endometrium (6).

AIMS AND

OBJECTIVES

AIMS AND OBJECTIVES

1. To determine the histopathological patterns of endometrial curettings in women with abnormal uterine bleeding.

2. To categorise the causes of abnormal uterine bleeding according to age group and pattern of bleeding.

3. To find out Estrogen and Progesterone Receptor status of non-malignant and malignant endometrium in the perimenopausal age group.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE

Normal menstruation is characterised by bleeding from secretory endometrium following an ovulatory cycle. It lasts for a duration less than 5 days with an average interval of 28 days and blood loss around 35 ml (20–80 ml) (7).

Any uterine bleeding of large volume, longer duration, and irregular in frequency is termed as abnormal uterine bleeding.

Abnormal uterine bleeding that is not associated with any genital tract abnormalities, general or endocrinological diseases is termed as “dysfunctional uterine bleeding”.

The term Heavy Menstrual Bleeding (HMB) is used when bleeding interferes with the woman's quality of life in physical, emotional, social and maternal aspects.

Women of all age groups present to the gynaecologist with abnormal uterine bleeding. AUB occurs in 9-14% of women of reproductive, perimenopausal and postmenopausal age groups. It significantly impairs the quality of life and increases financial burden.

PHYSIOLOGY OF NORMAL MENSTRUATION

Any bleeding not fulfilling the requirements of normal menstruation is termed as “Abnormal uterine bleeding” (8).

At any menstrual cycle only one oocyte is released. This is followed by secretory phase. After a constant period of 14 days after ovulation, there is shedding of the secretory endometrium. This manifests as monthly menstruation. When an oocyte is fertilised and an embryo is implanted, the process of endometrial shedding stops.

Normal monthly menstruation in a woman indicates that the hypothalamo pituitary ovarian axis is intact. Interruption of the axis at any point leads to disordered menses (9). Hence an understanding of the physiology of menstrual cycle is mandatory.

MENSTRUAL CYCLE

Cyclical menstruation continues throughout the reproductive era of life with an average rhythm of 28 -67 days, inclusive of 4–6 days of bleeding (except pregnancy and lactation).

It can be classified into two cycles

1. Ovarian cycle
2. Endometrial cycle

OVARIAN CYCLE

During this cycle, a single follicle develops and matures. It then ovulates and the remaining cells form the corpus luteum.

It can be divided into three phases

1. Follicular phase
2. Ovulation phase
3. Luteal phase

FOLLICULAR PHASE

This is the first part of the ovarian cycle. The follicle stimulating hormone released from the pituitary stimulates the follicle which matures as a result. Under the influence of several hormonal autocrine and paracrine interloops only one follicle develops, while all others stop developing. This dominant follicle will continue to mature through the sequential stages of primordial, preantral, antral and preovulatory graffian follicle. The fully mature follicle is termed as tertiary (Graffian) follicle. This follicle contains the ovum. The average length of this phase is 14 days but it is not constant.

OVULATION PHASE

Ovulation is the process of release of a mature ovum from the ovarian follicle. A Sustained peak level of estrogen for 24–48 hours in the late follicular phase results in a LH surge from the anterior pituitary (positive feedback effect). This process starts around the 12^{th} day of the average cycle and may last 48 hours. The egg matures under the influence of LH and the wall of the follicle is weakened. This results in the release of secondary oocyte from the fully developed follicle. Ootid is formed from the secondary oocyte which then becomes a mature ovum.

LUTEAL PHASE

This phase starts after the ovum is expelled from the follicle. The remaining granulosa and theca interna cells change into lutein cells which increase in size and accumulate lipid inclusions. This gives them a yellowish appearance. The mass thus formed is called the corpus luteum. The average length is 14 days (constant phase)

Luteo follicular transition

This period extends from the demise of corpus luteum (fall of serum estradiol, inhibin and progesterone level) to the selection of a dominant follicle for the next cycle.

Several hormones are involved in different phases of the menstrual cycle. Their levels can be measured in plasma.

1. Follicle stimulating hormone
2. Lutinizing hormone
3. Estrogen
4. Progesterone

ENDOMETRIAL CYCLE

The endometrium is the lining epithelium of the uterine cavity above the level of the internal os. It is composed of surface epithelium, glands, stroma and blood vessels. The endometrium is an organ where complex interplay between immune, endocrine and vascular systems take place (10).

Two distinct divisions are established

1. Basal zone (stratum basalis)
2. Superficial functional zone

BASAL ZONE

It is about one-third of the total depth of the endometrium, supplied by the basal arteries uninfluenced by hormone. No cyclic changes are observed in this zone. The regeneration of all the components occur from this zone. It measures about 1 mm.

FUNCTIONAL ZONE

This zone is under the influence of the fluctuating cyclic ovarian hormones, estrogen and progesterone. The changes in different components during an ovulatory cycle has been traditionally divided into four stages.

1. Regenerative phase.
2. Proliferative phase.
3. Secretory phase.
4. Menstruation.

PROLIFERATIVE PHASE

Under the influence of estrogens, secreted in increasing quantities by the ovary during the first part of the cycle, the stromal cells and the epithelial cells proliferate. This phase lasts from 5^{th} day to 14^{th} day of a 28 day cycle,but subjected to variation under physiological conditions. The average endometrial thickness is 2-3mm.

Early(5-7days)

During this phase, the regenerating epithelium is thin. The glands are short and narrow with epithelial mitoses. Mitosis is also seen in the stromal cells (stromal cells are stellate or spindle shaped) (2).

Mid (8–10 days)

The glands are long and curving. The lining epithelium is columnar with variable stromal edema and frequent mitoses.

Late (11–14 days)

The glands are tortuous.Nuclear pseudostratification seen. The stroma is moderately dense and actively growing.

SECRETORY PHASE

The changes of the components are due to the combined effects of estrogen and progesterone liberated from the corpus luteum after ovulation. Thus progesterone can only act on the endometrium previously primed by the estrogen. The length of the secretory phase is constant at 14 days. This is due to precise and rhythmically involuting corpus luteum after ovulation. The endometrial thickness is maximum at this phase (6–8 mm).

An interval phase lasts from 14^{th} to 15^{th} day. No noticable changes are seen for 36–48 hours after ovulation (2).

Early secretory phase, (16–20)

Glandular changes are prominent in this phase. By 16th day subnuclear vacuoles appear. Regular vacuolation appears around the 17th day. Around 18th day vacuoles decrease in size. The lumen is filled with early secretions and the nucleus reaches base of the cell. At 19th day, few vacuoles persist and intraluminal secretions are seen . Pseudostratification and mitoses are absent. On 20th day, intraluminal secretions are maximum.

Mid- to late secretory phase (21–27 days)

Stromal changes are prominent in this phase. Varying degrees of secretory exhaustion is seen. On 21st day there is marked stromal edema. On 22nd day, stromal edema is at its peak - cells have "naked nuclei". On 23rd day, periarteriolar predecidual change is found and spiral arteries are prominent. On 24th day, predecidual change is prominent and stromal mitoses recur. On 25th day, predecidual differentiation starts beneath the surface epithelium and granular lymphocytes increase in number. On 26th day, predecidua starts to become confluent. On 27th day, granular lymphocytes are maximum. The sheets of predecidua become confluent and focal necrosis appear. Between 24–27 days, secretory exhaustion of glands is seen. The glands are tortuous with intraluminal tufts giving them a saw-toothed appearance. The luminal borders are ragged and filled with secretions. There is variable cytoplasmic vacuolization.

MENSTRUAL ENDOMETRIUM

Regression of the corpus luteum with a fall in the level of estrogen and progesterone is an invariable preceding feature of menstrual phase. There is a breakdown of endometrial glands and stroma. This is seen throughout the functional layer by the end of the 28th day. There is also fibrin thrombi in small vessels. The stroma is condensed and collapsed with necrotic debris. Neutrophilic infiltration is also seen (11). This inflammatory process is completely physiological and strictly regulated (12). The endometrium is 0.5mm thick.

REGENERATION

Before menstruation ceases, the regeneration of endometrium starts and is completed 2–3 days after the end of menstruation. The stromal ground substance re-expands. Thickness of the endometrium averages 2 mm (1).

ENDOMETRIAL ANGIOGENESIS

Endometrium is the only tissue in the body to undergo rapid growth followed by shedding in a cyclical manner. Endometrial angiogenesis depends on a delicate balance between factors that promote and inhibit blood vessel formation. Estradiol and progesterone control angiogenesis by stimulating or inhibiting growth factors. Both these hormones stimulate the production of VEGF (vascular endothelial growth factor), which helps in proliferation of endometrial vessels. Progesterone stimulates thrombospondin-1, which is responsible for the inhibition of blood vessel proliferation during the secretory

phase. Withdrawal of hormones estrogen and progesterone releases proteolytic enzymes into the extracellular matrix. These enzymes degrade the matrix including vessels resulting in menstrual shedding (13).

DEFINITIONS

Menorrhagia (hypermenorrhea)

Excessive (> 80 mL) and prolonged (>7 days) bleeding occurring at regular intervals.

Polymenorrhea

Cyclic bleeding that occurs more frequently than every 21 days and persists in that frequency. If there is an associated increase in amount and duration of bleeding, it is called epimenorrhagia or polymenorrhagia.

Metrorrhagia

Cycles are irregular and can manifest as either contact bleeding or intermenstrual bleeding.

Menometrorrhagia

This term is applied when bleeding occurs erratically and excessively that the menstrual phase cannot be determined at all.

Oligomenorrhea

Cyclical bleeding that occurs at regular but long (>35 days) intervals.

Hypomennorhea

When the amount of menstrual bleeding is abnormally small and lasts for less than 2 days.

Intermenstrual bleeding

This refers to bleeding (usually not excessive) that occurs between otherwise normal menstrual cycles.

Precocious menstruation

Denotes the occurrence of menstruation before the age of 10 years.

Postcoital bleeding

Denotes vaginal bleeding after sexual intercourse.

EFFECTS OF STEROID HORMONES ON THE ENDOMETRIUM

Estrogens and progesterone are sex steroids synthesised from cholesterol. Mainly progesterone and testosterone are produced first in the ovaries. FSH acts on the granulosa cells of the ovary to stimulate aromatase. This enzyme converts testosterone and progesterone into estrogens. The principal and the most potent estrogen secreted by the ovaries is β-estradiol.

The size of the uterus increases twofold to threefold after puberty, but more important than the increase in uterus size are the alterations that are produced in the uterine endometrium under the influence of estrogens. This hormone increases the proliferation of the endometrial stroma. The endometrial

glands also become well developed. This helps in providing nourishment to the implanted ovum.

Very low levels of estrogen leads to endometrial atrophy, whereas high levels lead to hyperplasia.

Estrogen receptors are located in the nucleus. There are two types of estrogen receptors ER α and ER β. These receptors are encoded by two genes, namely ESR1 for ER α, and ESR2 for ER β. ER α is present most plentifully in the female genital tract, whereas ER β is expressed most abundantly in the prostate and ovaries.

Estrogen receptors are present in both the cytoplasm and the nucleus. However, the important functions of estrogen are mediated by the interaction with nuclear receptors. Estrogen receptors are bound with a large group of proteins called chaperones. When estrogen enters the cell and starts to bind with the receptors, these proteins dissociate. After binding of estrogen with their receptors, dimerization of the receptors occur. Dimers then bind to estrogen responsive elements in the target genes.

The levels of receptors to these hormones (estrogen and progesterone) are independent prognostic factors for endometrial carcinoma. Patients who have high levels of these receptors survive longer than patients whose receptor levels are low. Liao et al reported that, even for patients with lymph node metastases, the prognosis was significantly improved if the tumor was receptor positive. PR

appears to be a stronger predictor of survival than ER and at least for the ER, the absolute level of receptors may be important; the higher the level, better the prognosis (14).

METHODS OF ENDOMETRIAL SAMPLING

DILATATION AND CURETTAGE (D&C)

For decades, diagnostic curettage has been the most common operation performed on women. The procedure is not without its limitations. Hemorrhage, infection, and uterine perforation may occur and, because cervical dilatation is painful, the risks associated with the necessary general anesthetic are also present.

ENDOMETRIAL BIOPSY

Removal of a single strip of endometrium may be undertaken as an outpatient procedure, without cervical dilatation or general anesthetic. This technique is rarely used.

VABRA ASPIRATOR

This is a suction curette device composed of a 3–4 mm diameter steel cannula that has an opening on one side of its bent tip. The endometrial tissue is obtained by suction with an attached syringe. The amount of material this procedure captures varies.

PIPELLE BIOPSY

This is probably the most widely used outpatient method in the United States and Europe to sample the endometrial cavity. This procedure is quick and causes significantly less pain than Novak curette or Vabra aspirator. Although it produces less tissue, the diagnostic accuracy of the Pipelle biopsy is similar to that of the Vabra aspirator. It is no less reliable than other techniques for identifying endometrial carcinoma, although some studies have suggested a poor pick-up rate for early, low-volume tumors.

ENDOMETRIAL RESECTION

Transcervical resection of the endometrium is one of the different methods used for endometrial ablation. It is used as a conservative management of abnormal uterine bleeding. It should be done only after excluding hyperplasia and carcinoma by other methods of sampling like hysteroscopic biopsy or D&C. The endometrium should be supressed hormonally before doing this procedure. The tissue obtained is composed mainly of myometrial tissue. However, adenomyosis cannot be reliably diagnosed by this procedure.

ADEQUACY OF SPECIMEN

A scant specimen is a problem encountered frequently by pathologists because of the widespread use of techniques like pipelle biopsy. An adequate sample is widely obtained in late proliferative, late secretory, hyperplasias and carcinomas. A scant specimen is commonly seen in postmenopausal atrophy. Nevertheless, a scant specimen cannot rule out hyperplasia or carcinoma, as

cases have been reported in which biopsy has been scanty while subsequent hysterectomy has revealed carcinoma.

It is not necessary to repeat the biopsy when a scant tissue is noted. The specimen can be deemed as adequate even when a small amount of endometrial tissue is found. It is advisable to use the term unassessable rather than inadequate when a scant tissue is seen. McCluggage classified endometrial specimens into “inadequate” (no tissue is obtained) and “unassessable” (scant tissue is present). This classification holds little significance as the final clinical diagnosis between the two categories doesn’t differ significantly (15). The findings of other investigations like ultrasound and hysteroscopy should be taken into account before going for repeat biopsy in such cases. If the clinical features and other investigations point to some pathology, then D&C should be done (5).

CAUSES OF AUB

The term Dysfunctional uterine bleeding was previously used to denote heavy menstrual bleeding without any organic cause. The term Abnormal Uterine Bleeding was introduced by FIGO in 2011 to include all abnormal uterine bleeding with or without any organic lesion. The newer classification system is known by the acronym **PALM–COEIN** (16).

CLASSIFICATION OF AUB

Contrary to the PALM group, the COEIN group cannot be detected by imaging and histopathology.

CLASSIFICATION OF AUB (FIGO- 2011)			
Structural causes (PALM)		**Non structural systemic causes (COEIN)**	
Polyp	AUB-P	Coagulopathy	AUB-C
Adenomyosis	AUB-A	Ovulatory dysfunction	AUB-O
Leiomyoma - Submucosal myoma - Other myoma	AUB-L AUB-L SM AUB-LO	Endometrial	AUB-E
Malignancy and hyperplasia	AUB-M	Iatrogenic	AUB-I
		Not yet identified	AUB-N

The PALM group includes 4 causes that can be detected by imaging or histopathology, whereas the COEIN group includes causes that cannot be detected by these modalities (17).

Polyp (AUB-P)

Polyps can be detected by ultrasound, hysteroscopy or histopathology. They can be subdivided on the basis of number, size, location and histology.

Adenomyosis (AUB-A)

It can be diagnosed by ultrasound or MRI. It is further subdivided on the basis of the depth of myometrial invasion. Most often, it is asymptomatic and an incidental finding in hysterectomy specimens.

Leiomyoma (AUB-L)

Leiomyomas usually are not the cause of abnormal uterine bleeding. Mostly they are incidental findings. Myomas that are causal in abnormal bleeding usually involve the uterine cavity. They are further subdivided into primary, secondary and tertiary groups based on their number, size and location.

Malignancy and pre-malignant lesions

It is rare in reproductive age group. In this age group, it occurs usually in the setting of polycystic ovarian disease and chronic anovulation. Diagnosis is made by histopathological examination of the endometrium (D/C, biopsy).

Coagulopathy (AUB-C)

Coagulopathies are the cause of AUB in 13 to 20 % of women in the reproductive age group. The most common cause is Von Willebrand's disease.

Ovulatory disorders (AUB-O)

Ovulatory disorders are the cause of AUB in 20% of cases. These are the result of "Luteal – out – of – phase" events (LOOP) with deficient progesterone. Hypothyroidism and hyperprolactinemia are other causes.

Endometrial causes (AUB-E)

Endometrium normally produces prostaglandins from arachidonic acid, which is a fatty acid. Of these, PGE2 and PGI2 are vasodilators and antiplatelet aggregates. PGF2a and thromboxane A2 cause vasoconstriction and platelet aggregates. Progesterone is responsible for the secretion of PGF2a. In

anovulatory cycles, the absence of progesterone and thereby of PGF2a causes menorrhagia. Rare endometrial causes of AUB include tuberculous endometritis and infection, especially chlamydia.

Iatrogenic (AUB-I)

It is caused by steroidal hormones administered as oral contraceptives or IUCD. Copper T may cause "break-through bleeding" or menorrhagia. Other drugs causing abnormal bleeding include anticoagulants, phenothiazines and tricyclic antidepressants.

Not- classified (AUB-N)

This includes rare causes like arteriovenous malformations, varicose veins of uterine vessels, myohyperplasia and cases for which no cause can be identified by routine investigations

AUB CAN BE ACUTE OR CHRONIC

Acute bleeding- may occur sporadically (de novo) or may be superimposed on chronic AUB, and requires immediate treatment.

Chronic AUB - Abnormal menstrual bleeding related to volume, timing, regularity and duration of bleeding that lasts for 6 months (minimum 3 months), and requires thorough investigations.

DYSFUNCTIONAL UTERINE BLEEDING

The term Dysfunctional Uterine Bleeding is used once the organic causes of abnormal bleeding has been excluded. Upto 50% of women with abnormal bleeding have DUB (18) . DUB can be classified into

1. Ovulatory – 10 to 20%
2. Anovulatory – 80 to 90%

OVULATORY BLEEDING

Ovular bleeding can present as either polymenorrhea or menorrhagia.

Polymenorrhea

It usually occurs following childbirth and abortion, during adolescence and premenopausal period, and in pelvic inflammatory disease. This is due to shortening of follicular phase due to hyperstimulation by FSH or premature lysis of the corpus luteum. Endometrial study prior to or within few hours of menstruation reveals secretory changes

Menorrhagia

Two types are seen

Irregular shedding of the endometrium

This is due to incomplete and slow degeneration of the corpus luteum (Halban's disease). Endometrial sampling performed after 5th or 6^{th} day of the onset of menstruation reveals a mixture of secretory and proliferative endometrium.

Irregular ripening of the endometrium

This is due to the poor formation and function of the corpus luteum. Endometrial study prior to or soon after spotting reveals patchy areas of secretory changes amidst proliferative endometrium.

ANOVULATORY UTERINE BLEEDING

Continued exposure to estrogen in the presence of anovulation leads to marked endometrial proliferation. After a certain extent, the endometrium cannot support the proliferation and shedding occurs called as “anovulatory shedding”. This should be differentiated from the normal menstrual shedding. The absence of secretory exhaustion and presence of fibrin clots distinguishes anovulatory shedding from menstrual endometrium. Also in anovulation the glands lose their uniformity in size, shape and distribution leading to a pattern called disordered proliferative endometrium. It also leads to cystic dilatation of the glands and tubal metaplasia. (19). The underlying cause is unknown. Presumably, the failure of ovulation reflects an abnormal gonadotrophin stimulus.

Metropathia Haemorrhagica

It is a specialized form of anovulatory AUB, seen in women between 40 and 45 years. The basic fault may lie in the ovaries or may be due to a disturbance of the rhythmic secretion of the gonadotropins. There is a slow increase in the secretion of estrogen but no negative feedback inhibition of FSH. The net effect is a gradual rise in the level of estrogen with a concomitant phase of amenorrhea for about 6–8 weeks. After a variable period, however, the estrogen level falls

resulting in the endometrial shedding with heavy bleeding. Histopathology shows thick endometrium with polypoidal projections. There is cystic glandular hyperplasia. Some of the glands are small, others are large giving the appearance of “Swiss cheese” pattern.

SPECIFIC CAUSES OF ABNORMAL UTERINE BLEEDING

ENDOMETRITIS

Endometritis commonly occurs in the reproductive age group. It usually presents with abnormal uterine bleeding. Predisposing factors include recent pregnancy, prior instrumentation, intrauterine devices and cervical stenosis. Endometritis may also coexist with polyps, fibroid, hyperplasia or endometrial carcinoma. The endometrium shows proliferative activity and glandular architectural distortion. There is surface breakdown similar to that seen in menstrual breakdown. In low power, the stromal cells show spindle appearance.

In acute endometritis, the predominant inflammatory cells are neutrophils, sometimes seen within the glandular lumina forming microabscesses. The characteristic finding of endometritis is the presence of plasma cells. Other inflammatory cells like neutrophils and lymphocytes can be present in normal endometrium. In chronic endometritis, lymphocytes are prominent sometimes forming lymphoid follicles. Endometrial surface and glandular epithelium may show metaplastic changes. Immunohistochemistry using VS38 or Syndecan can be used to differentiate plasma cells from the

endometrial stromal cells, which resembles plasma cells. Plasma cells show positivity to both the markers whereas stromal cells positive for only VS38.

EFFECTS OF EXOGENOUS HORMONAL AGENTS AND DRUGS

A wide variety of hormonal agents are used in women for various indications. The effects of the most common hormonal agents used are discussed below.

ESTROGEN ONLY HORMONE REPLACEMENT THERAPY

These are rarely used in women because of the risk of endometrial hyperplasia and adenocarcinoma. The morphological features include proliferative activity similar to disordered proliferation, endometrial hyperplasia or endometrioid adenocarcinoma. The risk of carcinoma increases with the dose and length of treatment and the adenocarcinoma which develops is usually of an early stage and low grade.

COMBINED ESTROGEN AND PROGESTIN HORMONE THERAPY

Combined therapy is preferred in women with uterus due to the disadvantages of estrogen only therapy (5). Estrogen and progestin combination may be given sequentially or simultaneously (continuously). In sequential therapy, the endometrium shows weakly proliferative activity during estrogen therapy and poorly develop secretory activity during progestin therapy. This regimen doesn’t completely abolish the risk of carcinoma and the risk of endometrial hyperplasia with sequential regimen is 5.4%. With continuous combined regimen, the endometrium shows atrophy or weak secretory activity.

This regimen reduces the risk of development of endometrial hyperplasia and carcinoma. Hence continuous combined regimen is preferred to sequential HRT in perimenopausal women and postmenopausal women.

PROGESTIN – ONLY COMPOUNDS

These are commonly prescribed for abnormal uterine bleeding, endometriosis, contraception and for endometrial protection in patients taking tamoxifen. They usually result in endometrial atrophy with predecidual changes or decidualisation of the stroma.

GONADOTROPHIN RELEASING HORMONE AGONISTS

These are usually used in the management of uterine fibroids and endometriosis. The continuous administration of GnRH agonists results in decreased production of FSH and LH thereby causing decreased production of estrogen by the ovaries. This results in shrinkage of uterine leiomyomas. The endometrium shows atrophy or weak proliferative activity.

ANDROGENS

These are used in the treatment of endometriosis, as HRT, menorrhagia and endometrial hyperplasia. The endometrium has weak secretory activity during the initial phase of treatment but with continued treatment, the endometrium shows atrophic changes

TAMOXIFEN

It is used in the prevention and treatment of breast cancer. In the breast, it acts as an estrogen antagonist, whereas in the endometrium it acts as a weak estrogen agonist. Tamoxifen is associated with a variety of benign and malignant lesions in the endometrium. Patients receiving treatment for longer duration and at higher doses are particularly at high risk. Benign lesions include polyps and hyperplasia. Tamoxifen associated polyps are larger in size. Malignant lesions seen with tamoxifen usage are endometrial adenocarcinoma, including both endometrioid and serous types and carcinosarcomas.

ENDOMETRIAL EPITHELIAL METAPLASIA

Metaplasias are alterations in which the normal endometrial epithelium is substituted by a different epithelium. Metaplasias are commonly associated with endometrial polyps, exogenous hormone therapy, intrauterine devices, chronic endometritis and pyometra. Endometrial metaplasias tend to be associated with epithelial hyperplasias or endometrial adenocarcinomas, but by themselves are non-neoplastic. WHO classification subdivides endometrial metaplasia into mucinous, squamous, ciliary, hobnail, eosinophilic, clear cell, surface syncytial, papillary proliferation, and Arias–Stella effect (20). Squamous and mucinous metaplasias are particularly common with endometrioid adenocarcinoma.The clear cell and papillary syncytial metaplasias must be differentiated from type 2 endometrial cancers or serous endometrial intraepithelial carcinomas. In serous EIC and serous endometrial cancers, immunohistochemistry reveals strong p53 immunoreactivity while ER is generally negative, whereas the majority of

epithelial metaplasias show weak p53 immunoreactivity and strong positivity for ER.

ENDOMETRIAL POLYPS

These are the cause of uterine bleeding in 2 to 23% of patients undergoing endometrial biopsy (21). Polyps can occur at any age, but are most commonly seen in the perimenopausal age group. Polyps represent circumscribed foci of hyperplasia of the endometrium secondary to hormonal stimulus. Hormone replacement therapy and tamoxifen are associated with an increased occurrence of polyps. More often the glands and stroma of polyps are non-functional and doesn't respond to hormonal stimulus. Hence, they do not show the cyclical changes seen in normal endometrium. Grossly, polyps may be single or multiple, sessile or broad based, pedunculated or attached to the endometrium by a slender stalk. The histological features of the polyps include the following

1. Polypoid pieces of tissue lined by epithelium on 3 sides
2. Stroma altered by fibrosis or excessive collagen
3. Glands are distended with crowding
4. Glands out of phase with the adjacent non-polypoidal endometrium ie. in a different phase compared with the adjacent endometrium
5. Blood vessels in the stroma have a thick wall.

Polyps associated with tamoxifen use are characteristically multiple, large and fibrotic and exhibit stromal decidualisation and mucinous metaplasia (22).

The differential diagnosis for polyps includes endometrial hyperplasia, endometritis, adenosarcoma and adenofibroma. The distinction with endometrial hyperplasia is made by examining the stroma. In hyperplasia, the stromal cells are active with large vesicular nuclei and occasional mitotic figures, whereas the stroma of a polyp is composed of spindle (fibroblast-like) cells and contains abundant extracellular connective tissue and large, thick-walled blood vessels. Malignant transformation of endometrial polyps is rarely encountered. They can present as either in-situ or invasive serous carcinomas (23).

ENDOMETRIAL HYPERPLASIA

Definition and classification

Hyperplasia is characterised by the multiplication of endometrial glands of various sizes and shapes which results in higher glandular to stromal ratio. There are many classification systems for endometrial hyperplasia. But only the Kurman and Norris classification system is commonly used and currently approved by the World Health Organization (WHO) (24). It takes into account both architectural and cytological features. It is classified into *simple* and *complex* based on architecture and into *typical* and *atypical* based on the cytology.

Kurman and Norris (1986) classification of endometrial hyperplasia

Hyperplasia

- Simple
- Complex

Atypical hyperplasia

- Simple
- Complex

WHO classification of endometrial hyperplasia

Hyperplasia without atypia

- Simple hyperplasia without atypia
- Complex hyperplasia without atypia

Atypical hyperplasia

- Simple atypical hyperplasia (very rare)
- Complex atypical hyperplasia

Clinical features

Endometrial hyperplasias are most commonly seen in the perimenopausal period. It also can be encountered in women in the reproductive age group. Hyperplasia develops as a result of unopposed estrogenic stimulation. The etiologies for hyperplasia include

1. Prolonged anovulation
2. Estrogen only Hormone Replacement Therapy
3. Obesity

4. Polycystic ovarian disease (Stein–Leventhal syndrome)

5. Granulosa and theca cell tumors of the ovary

All these causes have in common unimpeded estrogen stimulation.

Hyperplasias can also occur in postmenopausal woman. Endometrial atrophy is the most frequent etiology of AUB in this group of women. In one study of postmenopausal bleeding, atrophy was the commonest finding followed by hyperplasia and endometrial cancer (25).

Gross features

Gross pathological findings are non-specific. Usually the volume of curettings is large in hyperplasias. The color is white to tan. It may be seen as diffuse thickening or as localised projections into the endometrium, which sometimes mimics a polyp.

HYPERPLASIA WITHOUT ATYPIA

SIMPLE HYPERPLASIA

It resembles mid to late proliferative endometrium. The endometrial glands vary in size and shape. Some glands show cystic dilatations giving the appearance of “swiss-cheese” pattern. This is referred to in older classification as cystoglandular hypertrophy. But not all cystic glands are hypertrophied. Some cystic glands show atrophy which is called cystic endometrial atrophy (7). The stroma is abundant. The epithelial lining is pseudostratified, the nuclei are

elongated, chromatin is dispersed and nucleoli are less prominent. The epithelial lining shows little budding.

COMPLEX HYPERPLASIA

In complex hyperplasia, the glands are densely packed with back to back arrangement. The glandular structures are increased in relation to the stroma, which is decreased. The glands show more structural complexity with more branching in the form of outfoldings and inpouchings. Cytologically the glandular epithelial cells are identical to that of simple hyperplasia.

ATYPICAL HYPERPLASIA

The presence of atypical nuclei is an important finding due to the risk of development of carcinoma. Atypical nuclei are rounded, pleomorphic, show stratification with loss of polarity and have condensed chromatin with prominent nucleoli giving a vesicular appearance. Atypia may not be seen in all glandular epithelial cells. Occasional atypical cells can be ignored. Metaplastic changes are often found in association with atypical hyperplasia. The presence of histiocytes in the stroma gives a clue to diagnose hyperplasia in asymptomatic postmenopausal women.

ENDOMETRIAL INTRAEPITHELIAL NEOPLASIA (EIN)

EIN comes under a different type of classification system of hyperplasia. It is a premalignant lesion for endometrial carcinoma. It is diagnosed on the basis of clinical, histomorphometric, molecular and genetic factors. EIN represents monoclonal proliferation of cells with growth advantage conferred by mutations.

These cells are able to grow without hormonal support. Although EIN cannot be equated with a single diagnosis in WHO classification, it mostly corresponds to complex atypical hyperplasia followed by complex hyperplasia.

Differential diagnosis

These includes disordered proliferative phase, tubal metaplasia, polyps, cystic atrophy and endometrial breakdown. Atypical hyperplasia should be differentiated from well differentiated adenocarcinoma and atypical polypoid adenomyoma. Distinction between atypical hyperplasia and adenocarcinoma is made out by looking for the stromal invasion which is present in the latter.

Behaviour

Hyperplasia without atypia usually regress. Atypical hyperplasia is associated with a high risk of developing adenocarcinoma. In one study, 23% of atypical hyperplasia progressed to carcinoma whereas in the absence of atypia the risk of progression to carcinoma decreases to 2% atypia (26). If adenocarcinoma develops from atypical hyperplasia, it is usually well differentiated and focal with little invasion of the myometrium. It is important to note that adenocarcinoma may be co-existant with CAH (25%) (found on hysterectomy) or may evolve from hyperplasia (30%). Age of the patient is also an important factor influencing the behaviour of hyperplasia. Most of the simple hyperplasia in young women regress.

Relationship with carcinoma

1. Most cases of endometrial carcinoma of the endometrioid type are preceded by a stage of hyperplasia.
2. Overall, relatively few patients with hyperplasia will subsequently develop cancer. Rather, the majority of the cases are responsive to progestin treatment.
3. The more severe the hyperplasia, the more likely it is to be followed by (or to be concurrent with) carcinoma.

MANAGEMENT OF HYPERPLASIA

The factors which determine the treatment of endometrial hyperplasia include the age of the patient, the histologic type and fitness for surgery (especially in postmenopausal women).

PREMENOPAUSAL WOMEN

Distinguishing between CAH and endometrial adenocarcinoma is very important especially in premenopausal women who wish to retain their fertility. Premenopausal women with abnormal bleeding should be considered for endometrial biopsy only if they have risk factors like polycystic ovarian disease or obesity as there is a low risk of having carcinoma in this age group. Hyperplasia without atypia can be treated conservatively with cyclical progestin. They should be followed up after 6 months with endometrial sampling to look for regression (26). Women with atypical hyperplasia can be treated with progestin suppression if they wish to retain their fertility. However, they should

have close follow-up with periodic endometrial samplings. Conservative management can also be offered to women with well differentiated carcinoma. Hormonal therapy with progestin for 9 months resulted in the regression of lesions in 75% of women with carcinoma (27).

PERIMENOPAUSAL WOMEN (40 – 55 YEARS)

These women should be considered for an endometrial biopsy even though there is also at low risk of developing carcinoma. Women with atypical hyperplasia in this age group should be started on hormonal therapy with progestins. However, they should be followed up with endometrial biopsies every 3 months. Hysterectomy should be performed when hyperplasia persists in follow-up biopsy.

POST MENOPAUSAL WOMEN (OVER 55 YRS OF AGE)

Women in this age group have a significantly higher risk of developing adenocarcinoma or atypical hyperplasia. Endometrial biopsy should be performed followed by fractional curettage if hyperplasia is present. If hyperplasia without atypia is detected on curettage, conservative management includes observation only or treatment with progestin. Repeated episodes of irregular bleeding unresponsive to hormonal treatment requires hysterectomy. If atypical hyperplasia is detected, hysterectomy is the management of choice. In women unfit for surgery, continuous treatment with progesterone acetate can be used to avoid surgery. For postmenopausal women on exogenous estrogens who show hyperplasia on biopsy, termination of treatment is usually sufficient to

cause regression. Alternatively, a cyclical or continuous administration of medroxyprogesterone can be considered to reduce the risk of carcinoma.

ENDOMETRIAL INTRAEPITHELIAL CARCINOMA (EIC)

EIC is the precursor of serous endometrial carcinoma. It is an intraepithelial malignancy with focal or diffuse involvement of the surface and glandular epithelium. The nuclei are hobnail shaped and show marked atypia. Sometimes they are associated with metastatis, especially to peritoneal surfaces. Hence they are not in situ carcinomas. The presence of disseminated disease is an important prognostic factor. So Wheeler et al combine EIC with serous carcinom measuring < 1 cm and gave the terminology “minimal uterine serous carcinoma” (28) . They can be differentiated from serous carcinoma by the absence of stromal invasion. It usually occurs in the setting of endometrial atrophy seen in older, postmenopausal women. EIC is often present on the surface of a polyp. Immunohistochemistry shows intense reactivity for p53.

Behaviour

EIC commonly coexists with invasive carcinoma, usually serous type. EIC or serous carcinoma without evidence of metastasis has a very good prognosis. The presence of evidence of extrauterine disease implies a bad prognosis. Hence, it is important to do a thorough staging at the time of hysterectomy when a diagnosis of EIC is made by biopsy.

CARCINOMA OF THE ENDOMETRIUM

Endometrial carcinoma has emerged as the commonest gynaecologic malignancy in developed countries. This is because of the increased incidence of risk factors like obesity and longer survival of women (29). However, in developing countries cervical cancer continues to be the commonest malignancy of the genital tract. Endometrial carcinoma usually presents in the early stages with abnormal vaginal bleeding. Hence they are amenable to curative therapy by hysterectomy. It is mainly a disease of postmenopausal women.

ENDOMETRIAL ADENOCARCINOMA, ENDOMETRIOID TYPE (TYPE I)

These are the most common type of endometrial cancers accounting for about 80% of cases. They usually occur in 55- 65 years of age, slightly younger than type II cancers. They usually occur in association with the estrogen related risk factors described below (30). The precursor lesion is atypical hyperplasia or endometrial intraepithelial neoplasia. These tumors are usually of low grade. They are less invasive and have less propensity for lymphatic spread. The prognosis is generally good. The genetic alterations include PTEN mutations, microsatellite instability and K-ras mutation.

ENDOMETRIAL ADENOCARCINOMA, NON-ENDOMETRIOID TYPE (TYPE II)

Non-endometrioid tumors occur in older, postmenopausal women, and account for 10–20% of endometrial carcinomas. They are not associated with

clinical evidence of estrogen stimulation, and usually arise from atrophic endometrium. These tumors include serous carcinoma, clear cell carcinoma and other histologic subtypes. They are usually poorly differentiated (grade 3) tumors. They arise frequently in the setting of endometrial polyps. They have rapid courses, a high degree of nuclear pleomorphism and frequent aneuploid DNA content. These tumors are aggressive with deeper myometrial invasion and increased risk of lymphatic dissemination. The prognosis is generally poor. Mutations in the tumor suppressor TP53 are present in at least 90% of serous endometrial carcinoma.

A modified version of the recent World Health Organization (WHO) and International Society of Gynecological Pathologists (ISGYP) classification of endometrial carcinoma is shown below.

CLASSIFICATION OF ENDOMETRIAL CARCINOMA

1. Endometrioid adenocarcinoma
2. Serous carcinoma
3. Clear cell carcinoma
4. Mucinous carcinoma
5. Villoglandular
6. Secretory
7. Ciliated cell
8. Endometrioid adenocarcinoma with squamous differentiation
9. Squamous carcinoma

10. Mixed types of carcinoma
11. Undifferentiated carcinoma

RISK FACTORS FOR ENDOMETRIAL CARCINOMA

ESTROGENS

Estrogens are an important stimulus for the development of endometrial hyperplasia and adenocarcinoma. The widespread use of estrogens in HRT for peri and post menopausal women has resulted in a sudden rise in the incidence of endometrial cancers. The risk of developing endometrial cancer is elevated three- to sixfold in women taking unopposed estrogens (31), rising to 9.5-fold if unopposed estrogen has been used for 10 years or longer (32). The increase risk can be alleviated by the addition of progestins for 7 to 10 days a month in women taking estrogen for HRT.

TAMOXIFEN

Tamoxifen is a selective estrogen receptor modulator used as adjuvant therapy for breast cancer. In women of child-bearing age, it antagonises estrogens, whereas in post-menopausal women, it has a weak estrogenic effect. Tamoxifen administration is associated with an overall slightly increased risk (two to three times) of endometrial adenocarcinoma (33).

POLYCYSTIC OVARY SYNDROME (PCOS)

PCOS is characterised by atleast two of the following features: anovulation or infrequent ovulation, androgen excess, and polycystic ovaries. The patients are usually infertile, have elevated estrogen levels, and associated

insulin resistance may cause type 2 diabetes. Endometrial carcinoma occurs in less than 5% of those women with polycystic ovaries (34).

OBESITY

It is a significant risk factor for the development of endometrial cancer. The increase risk may be due to increased peripheral conversion of androgens to estrogens (estrone and estradiol) in adipose tissue and decreased levels of serum sex hormone binding globulin (SHBG).

SEX CORD-STROMAL TUMORS

Granulosa cell tumors and thecoma are associated with a prolonged, excessive and unopposed estrogen production. This produces endometrial hyperplasia, EIN and endometrial carcinoma. 9–13% of women with granulosa cell tumors develop endometrial carcinomas (35).

NON-NEOPLASTIC OVARAIN LESIONS

Endometrial carcinoma is found in over one-third of women with diffuse hyperthecosis.

REPRODUCTIVE FACTORS

Nulliparity is a strong risk factor for endometrial carcinoma. Infertility, particularly when it is coupled with anovulation and progesterone deficiency is also a risk factor for development of endometrial adenocarcinoma. Early menarche, late menopause and low parity are factors associated with increased overall lifetime estrogen exposure.

SYNDROMES

Endometrial carcinoma can rarely be a manifestation of hereditary cancer syndromes like Hereditary Non-polyposis Colonic Cancer syndrome (HNPCC or Lynch syndrome) and Cowden syndrome.

The use of oral contraceptives reduces the risk of endometrial cancer in some studies by half (36). Cigarette smoking reduces the risk of endometrial carcinoma.

Clinical features

The peak incidence of endometrial carcinoma is in postmenopausal women between 55 -65 yrs of age. Carcinoma of the endometrium is rare in women under the age of 40. It usually presents with irregular or post menopausal vaginal bleeding.

Gross features

The tumor may be seen as diffuse endometrial thickening or commonly as one or more multiple exophytic growths with a shaggy appearance. Sometimes it may be a polypoidal growth. Myometrial invasion is accompanied by enlargement of the uterus. The cervix is involved in approximately 20% of cases.

Microscopic features

Endometrioid carcinoma demonstrates a glandular pattern resembling normal proliferative endometrium. The grading is based on the microscopic

appearance of the amount of solid growth of the glandular component. The cells are larger than cells of normal endometrium, show varying degrees of pleomorphism and prominent nucleoli. The nuclear grade is determined by the degree of anisonucleosis, chromatin distribution and size of the nucleoli. Assessment of myometrial invasion is important for staging the tumor. In the majority of cases myometrial invasion is accompanied by a desmoplastic stroma and inflammatory response. Whereas, some low grade tumors infiltrate the myometrium without stromal response.

The most recent revision of the FIGO (International Federation of Gynecology and Obstetrics) Staging System is given below. Grading of the tumor should be done (both architectural and nuclear grading) before classifying endometrial carcinoma using FIGO staging.

International Federation of Gynaecology and Obstetrics Staging of Endometrial Cancer, 2009 (5)

IA	G123	Tumor limited to the inner half of myometrium
IB	G123	Tumor invasion into the outer half of myometrium
II	G123	Tumor invades cervical stroma
IIIA	G123	Tumor invades serosa and/or adnexa
IIIB	G123	Vaginal and/or parametrial involvement
IIIC1	G123	Metastases to pelvic lymph nodes
IIIC2	G123	Metastases to paraaortic lymph nodes
IVA	G123	Tumor invasion of bladder and/or bowel mucosa
IVB	G123	Distant metastases including intraabdominal and/or inguinal lymph nodes

METHODOLOGY

METHODOLOGY

The prospective study was conducted at the Department of pathology at Karpaga Vinayaga Institute of Medical Sciences, Chinna Kolambakkam for a period of two years from August 2013 to September 2015. The study was approved by the Institutional Ethics Committee. The study was conducted on 150 consecutive endometrial samples obtained by dilatation and curettage.

Patients presenting to the gynaecology OPD with symptoms of abnormal uterine bleeding were selected. Complete history including drug history was taken. A complete general examination was done. Routine investigations like complete blood count, bleeding time, clotting time and Chest X-ray were done. Ultrasound abdomen and pelvis was performed by an experienced sonologist.

IMMUNOHISTOCHEMISTRY

Endometrial samples of 41 premenopausal women which were histopathologically diagnosed as proliferative, simple hyperplasia, complex hyperplasia, atypical hyperplasia and endometrial adenocarcinoma were analysed immunohistochemically for ER and PR expression.

INCLUSION CRITERIA

Patients with abnormal vaginal bleeding aged > 18 years who presented to the gynaecology department were included.

EXCLUSION CRITERIA

Patients with systemic diseases, genital tuberculosis, IUCD in situ, incomplete history, inadequate samples, bleeding and coagulation defects, pregnancy complications like abortion, molar pregnancy, ectopic pregnancy and patients on antiplatelet drugs were excluded.

COLLECTION OF SPECIMEN

Patients recruited into the study were admitted and endometrial curettage was performed by a gynaecologist. The tissue samples were received in 10% formalin and sent to the pathology department. After routine processing, tissue sections of 4-6 microns were cut and stained with eosin and haematoxylin. The slides were seen under the light microscope by pathologists and studied for their histomorphological patterns. Four micron thick representative tissue sections were immunohistochemically stained for ER and PR using a combination of HRP and pressure cooker antigen retrieval was used (tris-EDTA buffer- pH 6) and analysed for positivity of receptors in the glandular epithelium.

STATISTICAL METHODS

Data were entered in Microsoft excel and managed using SPSS software version 16. Patients were categorised into three age groups, namely reproductive age group (18-40 yrs.), perimenopausal age group (41-50 yrs.) and post-menopausal age group (>50 yrs.). Analysis was done in the form of percentages and proportions and represented in tables and graphs.

RESULTS

RESULTS

A total of 150 patients underwent diagnostic D&C for AUB during the study period and the curettage was submitted for histopathological examination. The age of the patients studied were categorized into three groups, namely reproductive, perimenopausal and post-menopausal. Patients with AUB ranged from 23 to 65 years with a mean age of 42.6 years and a median age of 42 years. Maximum patients (49 %) with abnormal uterine bleeding presented in age group 41-50 years closely followed by 42% in the reproductive (18-40 years) age group. The menopausal age group constituted 13% of patients.

Table-1. Age group of patients presenting with AUB

Age group (years)	Total	%
18 - 40 years (reproductive)	63	42
41 - 50 years (perimenopausal)	74	49
> 50 years (postmenopausal)	13	9
Total	150	100

Graph-1. Age group of patients presenting with AUB

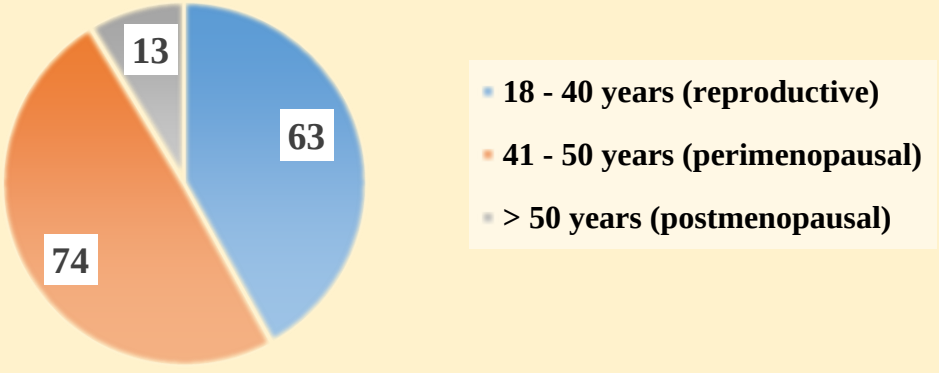
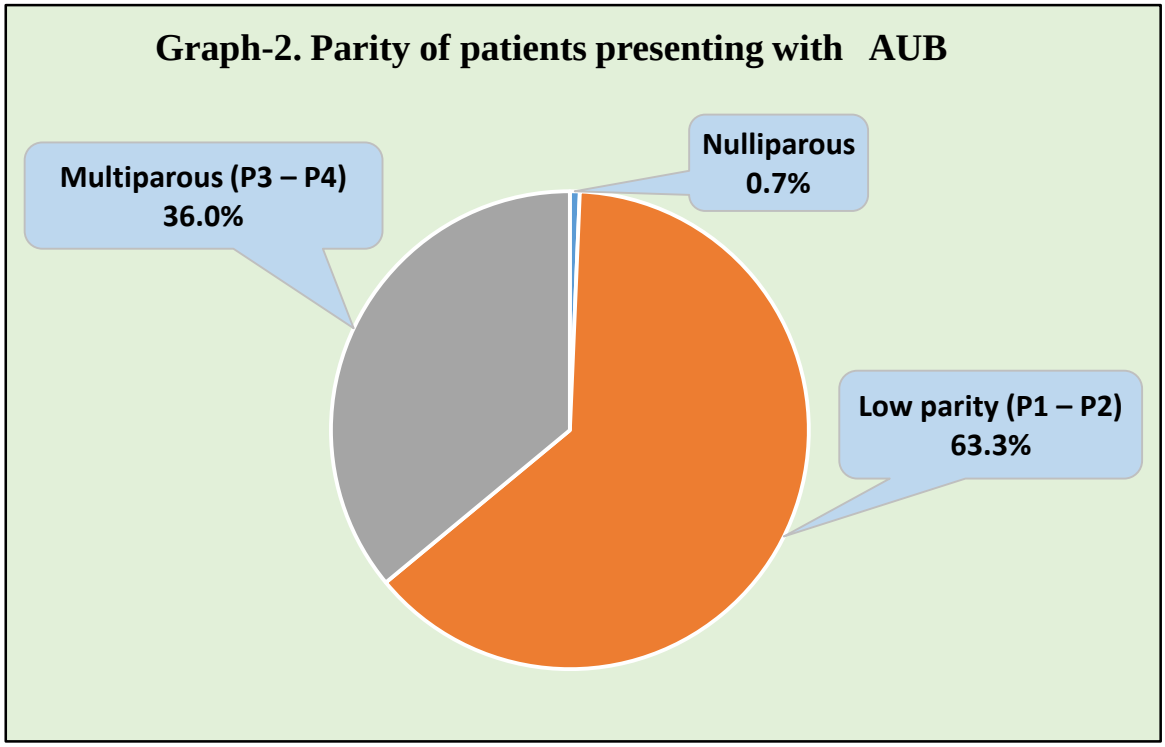


Table-2. Parity of patients presenting with AUB

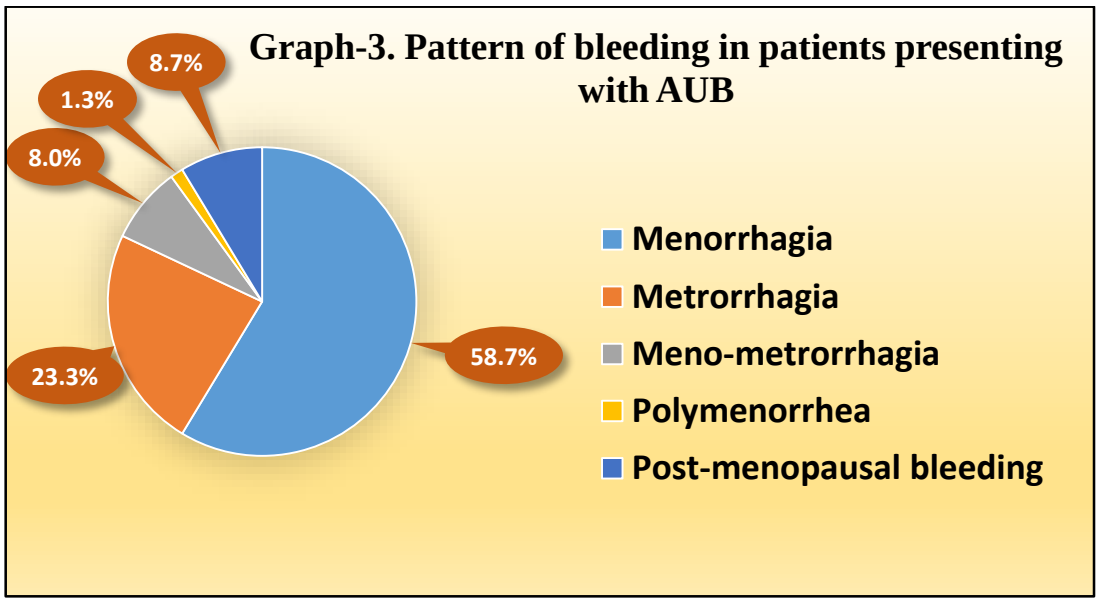
S.№	Parity	Number	Percentage (%)
1	Nulliparous	1	0.7
2	Low parity (P1 – P2)	95	63.3
3	Multiparous (P3 – P4)	54	36
	Total	150	100



Of these 150 patients, 63.3% of patients are of low parity (P1 or P2), 36% of patients were multiparous and only one patient (0.7 %) was nulliparous.

Table-3. Pattern of bleeding in patients presenting with AUB

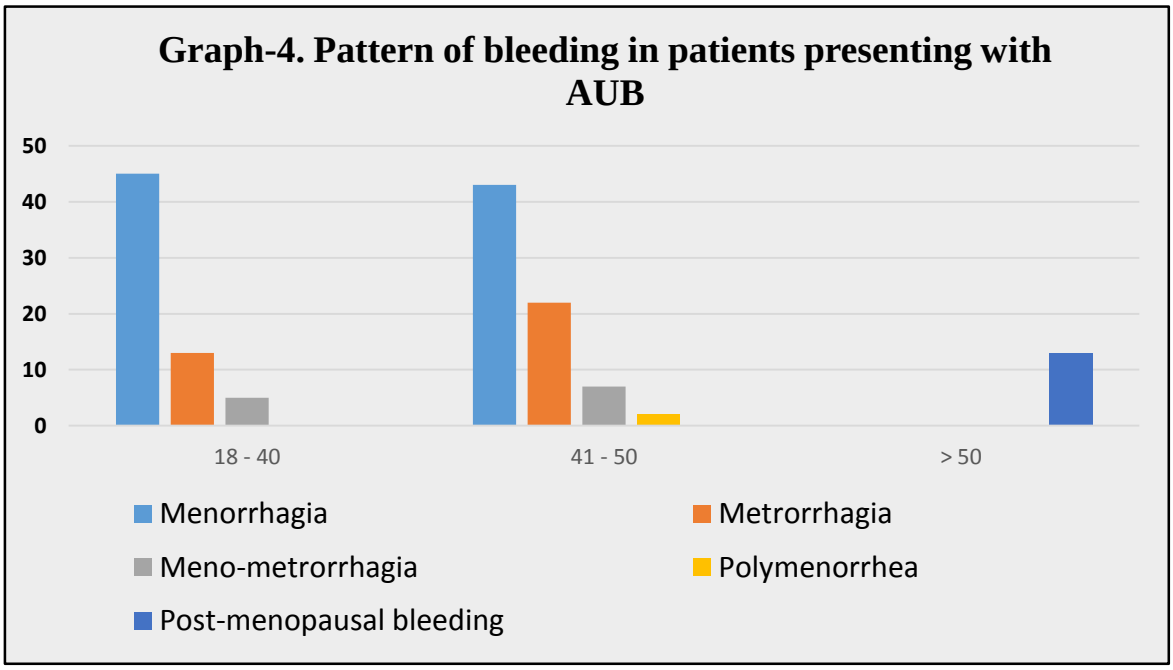
S.№	Pattern of bleeding	number	%
1	Menorrhagia	88	58.7
2	Metrorrhagia	35	23.3
3	Meno-metrorrhagia	12	8.0
4	Polymenorrhea	2	1.3
5	Post-menopausal bleeding	13	8.7
	Total	150	100.0



The most common complaint was menorrhagia (58.7%), followed by metrorrhagia (23.3%). Meno-metrorrhagia constituted 12% and postmenopausal bleeding is seen in 8.7% of patients. Polymenorrhea was rare, seen in 2 (1.3%) patients.

Table-4. Pattern of bleeding in patients presenting with AUB

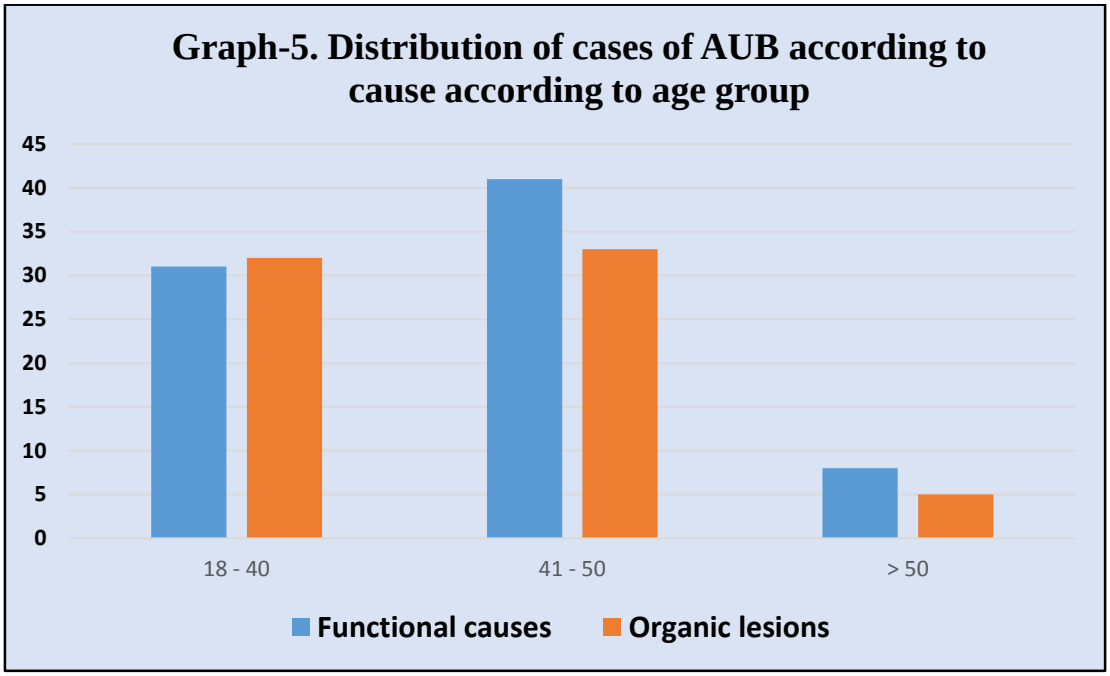
S.№	Pattern of bleeding	18 - 40	41 - 50	> 50	Total	%
1	Menorrhagia	45	43	0	88	58.7
2	Metrorrhagia	13	22	0	35	23.3
3	Meno-metrorrhagia	5	7	0	12	8.0
4	Polymenorrhea	0	2	0	2	1.3
5	Post-menopausal bleeding	0	0	13	13	8.7
	Total	63	74	13	150	100



Age specific analysis of the pattern of bleeding revealed that menorrhagia is the most common complaint in both the reproductive and perimenopausal age group followed by metrorrhagia. The second most common complaint in the reproductive and post-menopausal age groups were metrorrhagia.

Table-5. Distribution of cases of AUB according to cause according to age group

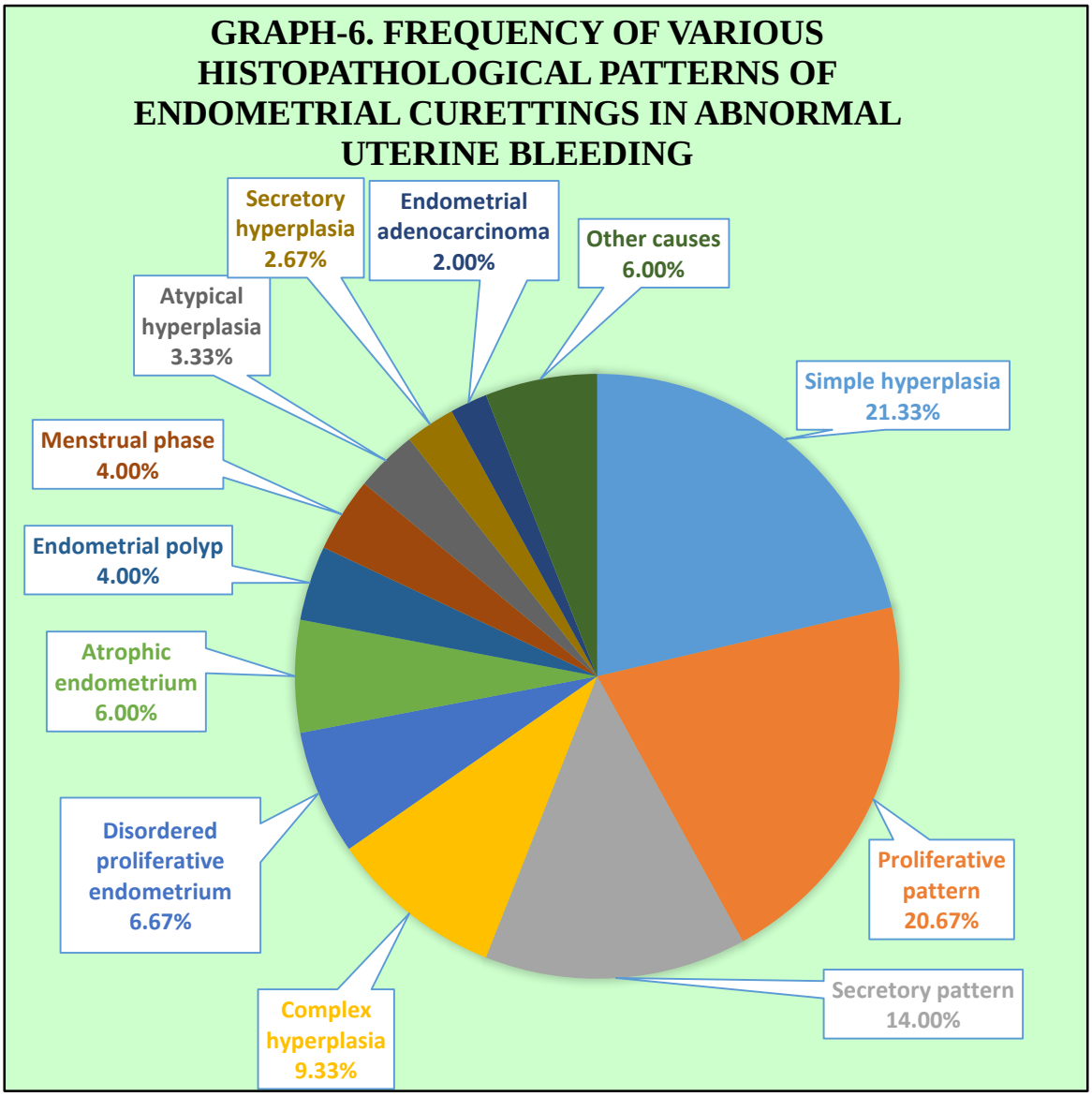
Cause of AUB	18 - 40	41 - 50	> 50	Total	%
Functional causes	31	41	8	80	53
Organic lesions	32	33	5	70	47
Functional/ Organic	0.96	1.24	1.6	1.14	-
Total	63	74	13	150	100



Evaluation of the endometrium revealed various patterns on histopathology (Table-6). Functional causes accounted for slightly more than half of the causes (53%). In the present study, the proportion of functional to organic causes increase as age increases (0.96 in reproductive age; 1.24 in perimenopausal and 1.6 in post-menopausal women).

Table-6. Frequency of Various Histopathological Patterns of Endometrial Curettings in Abnormal Uterine Bleeding

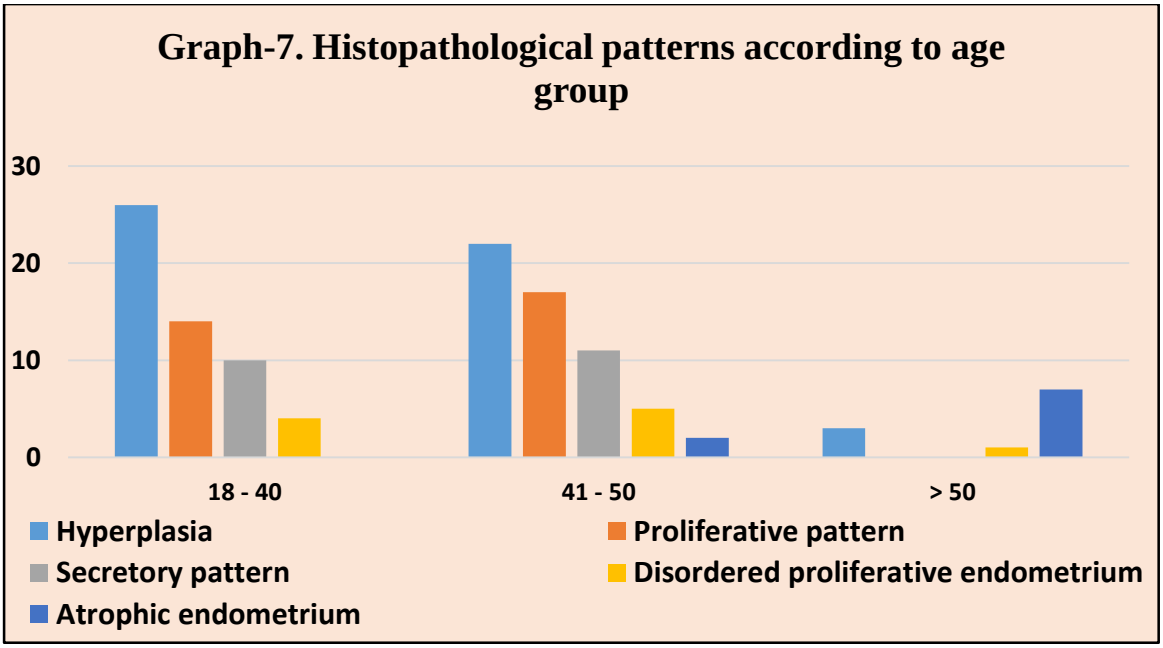
S.№	HISTOPATHOLOGICAL DIAGNOSIS	Total	%
1	Simple hyperplasia	32	21.33
2	Proliferative pattern	31	20.67
3	Secretory pattern	21	14.00
4	Complex hyperplasia	14	9.33
5	Disordered proliferative endometrium	10	6.67
6	Atrophic endometrium	9	6.00
7	Endometrial polyp	6	4.00
8	Menstrual phase	6	4.00
9	Atypical hyperplasia	5	3.33
10	Secretory hyperplasia	4	2.67
11	Endometrial adenocarcinoma	3	2.00
12	Chronic endometritis	2	1.33
13	Arias stella effect	1	0.67
14	Endometrial metaplasia	1	0.67
15	Granulomatous TB	1	0.67
16	Hormonal changes	1	0.67
17	Irregular shedding	1	0.67
18	Mixed pattern	1	0.67
19	Squamous cell carcinoma infiltrating endometrium	1	0.67
	Total	150	100



Overall, the commonest histopathological diagnosis was simple hyperplasia 21.3%), followed by the proliferative pattern (20.6%), secretory pattern (14%) complex hyperplasia (9%), disordered proliferative endometrium (6.6%), atrophic endometrium (6%), endometrial polyp (4%), menstrual phase (4%), atypical hyperplasia (3.3%), secretory hyperplasia (2.67%) and endometrial adenocarcinoma (2%).

Table-7. Histopathological patterns according to age group

S.№	HISTOPATHOLOGICAL DIAGNOSIS	Age group (years)			Total	%
		18 - 40	41 - 50	> 50		
1	Simple hyperplasia	18 (28.6%)	12 (16.2%)	2 (15.4%)	32	21.33
2	Proliferative pattern	14 (22.2%)	17 (23%)	0	31	20.67
3	Secretory pattern	10 (15.9%)	11 (14.9%)	0	21	14.00
4	Complex hyperplasia	6 (9.5%)	8 (10.8%)	0	14	9.33
5	Disordered proliferative endometrium	4 (6.3%)	5 (6.8%)	1 (7.7%)	10	6.67
6	Atrophic endometrium	0	2 (2.7%)	7 (53.8%)	9	6.00
7	Endometrial polyp	3(4.8%)	3 (4.1%)	0	6	4.00
8	Menstrual phase	3 (4.8%)	3 (4.1%)	0	6	4.00
9	Atypical hyperplasia	2 (3.2%)	2 (2.7%)	1 (7.7%)	5	3.33
10	Secretory hyperplasia	2 (3.2%)	2 (2.7%)	0	4	2.67
11	Endometrial adenocarcinoma	0	2 (2.7%)	1 (7.7%)	3	2.00
12	Chronic endometritis	0	2 (2.7%)	0	2	1.33
13	Arias stella effect	1 (1.6%)	0	0	1	0.67
14	Endometrial metaplasia	0	1 (1.4%)	0	1	0.67
15	Granulomatous TB	0	1 (1.4%)	0	1	0.67
16	Hormonal changes	0	1 (1.4%)	0	1	0.67
17	Irregular shedding	0	1 (1.4%)	0	1	0.67
18	Mixed pattern	0	1 (1.4%)	0	1	0.67
19	Squamous cell carcinoma infiltrating endometrium	0	0	1	1	0.67
	Total	63 (100%)	74 (100%)	13 (100%)	150	100.00



In the reproductive age group, the commonest histopathological diagnosis was simple hyperplasia (28.6%), followed by the proliferative pattern (22.2%), secretory pattern (15.9%) complex hyperplasia (9.5%) and disordered proliferative endometrium (6.3%).

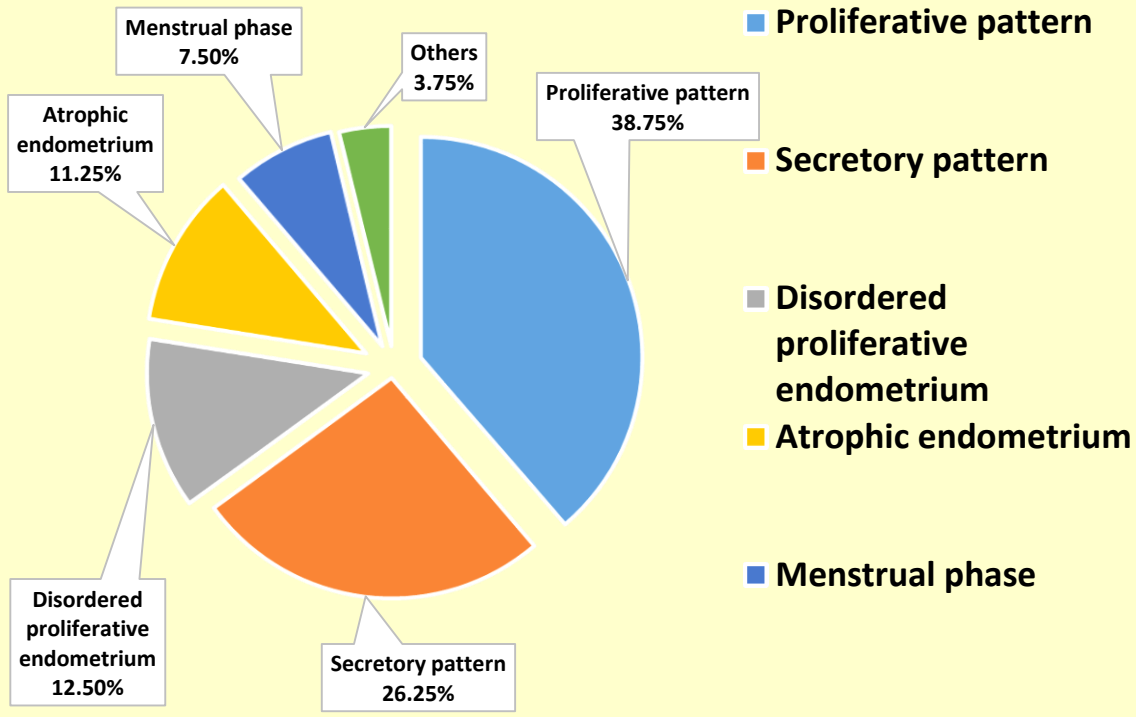
In the perimenopausal age group, diagnoses were proliferative pattern (23%) followed by simple hyperplasia (16.2%), secretory pattern (14.9%), complex hyperplasia (10.8%) and disordered proliferative endometrium (6.8%).

The commonest histopathological diagnosis in patients presenting with post-menopausal bleeding was atrophic endometrium (53.8%) followed by simple hyperplasia (15.4%), disordered proliferative endometrium (7.7%), endometrial adenocarcinoma (7.7%), atypical hyperplasia (7.7%) and squamous cell carcinoma infiltrating endometrium (7.7%).

Table-8. Abnormal uterine bleeding due to non-organic causes

S.№	HISTOPATHOLOGICAL DIAGNOSIS	Age group (years)			Total	%
		18 - 40	41 - 50	> 50		
1	Proliferative pattern	14	17	0	31	38.75
2	Secretory pattern	10	11	0	21	26.25
3	Disordered proliferative endometrium	4	5	1	10	12.50
4	Atrophic endometrium	0	2	7	9	11.25
5	Menstrual phase	3	3	0	6	7.50
6	Hormonal changes	0	1	0	1	1.25
7	Irregular shedding	0	1	0	1	1.25
8	Mixed pattern	0	1	0	1	1.25
	Total	31	41	8	80	100.00

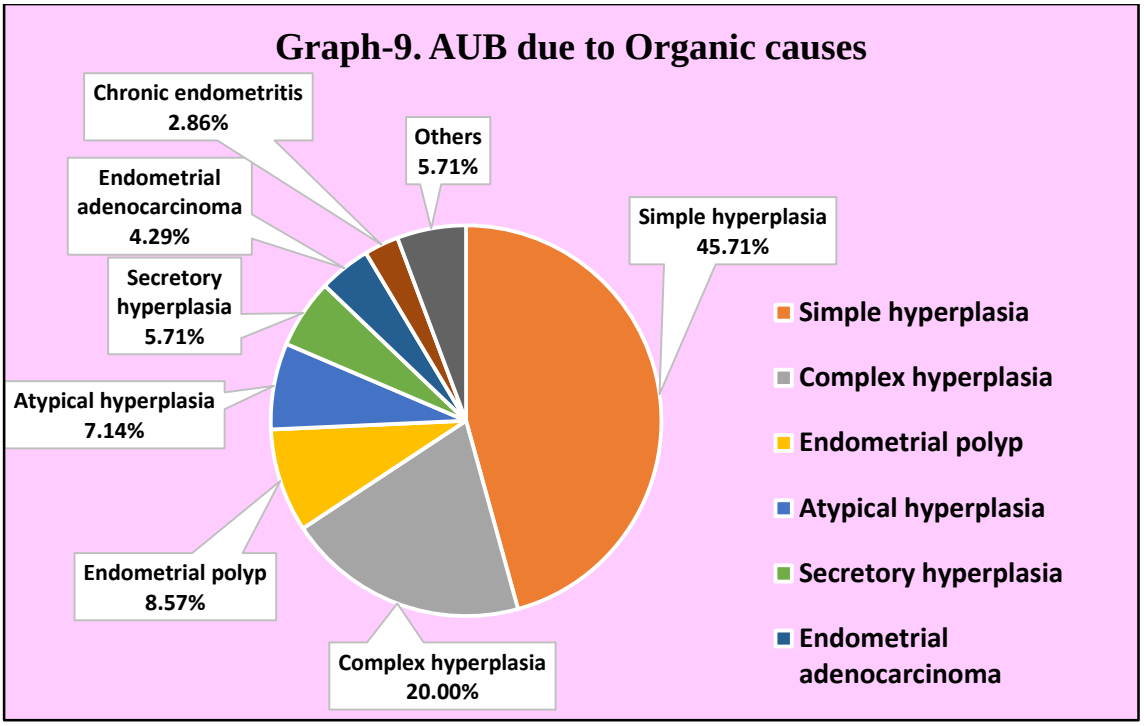
Graph-8. Abnormal uterine bleeding due to non-organic causes



The non-organic causes (in all age groups) in decreasing order of frequency is proliferative pattern (38.75%), secretory pattern (26.25%), disordered proliferative endometrium (12.50%), atrophic endometrium (11.25%), menstrual phase (7.5%), hormonal changes (1.25%), irregular shedding (1.25%), and mixed pattern (1.25%).

Table-9. Abnormal uterine bleeding due to Organic causes

S. №	HISTOPATHOLOGICAL DIAGNOSIS	Age group (years)			Total	%
		18 - 40	41 - 50	> 50		
1	Simple hyperplasia	18 (56.3%)	12 (36.4%)	2 (40%)	32	45.71
2	Complex hyperplasia	6 (18.8%)	8 (24.2%)	0	14	20.00
3	Endometrial polyp	3 (9.4%)	3 (9.1%)	0	6	8.57
4	Atypical hyperplasia	2 (6.3%)	2 (6.1%)	1 (20%)	5	7.14
5	Secretory hyperplasia	2 (6.3%)	2 (6.1%)	0	4	5.71
6	Endometrial adenocarcinoma	0	2 (6.1%)	1 (20%)	3	4.29
7	Chronic endometritis	0	2 (6.1%)	0	2	2.86
8	Arias stella effect	1 (3.1%)	0	0	1	1.43
9	Endometrial metaplasia	0	1 (3%)	0	1	1.43
10	Granulomatous TB	0	1 (3%)	0	1	1.43
11	Squamous cell carcinoma infiltrating endometrium	0	0	1 (20%)	1	1.43
	Total	32	33	5	70	100.00



The organic causes of abnormal uterine bleeding in this series diagnosed by histopathological examination of D&C specimens in decreasing order of frequency are simple hyperplasia (45.7%), complex hyperplasia (20%), polyps (8.5%), atypical hyperplasia (7.1%), secretory hyperplasia (5.7%), endometrial adenocarcinoma (4.2%), chronic endometritis (2.8%), Arias stella effect (1.4%), endometrial metaplasia (1.4%), granulomatous TB (1.4%) and squamous cell carcinoma infiltrating endometrium (1.4%).

Simple hyperplasia (56.3%) was the commonest organic cause in the reproductive age group followed by complex hyperplasia (18.8%), endometrial polyps (9.4%), secretory hyperplasia (6.3%), atypical hyperplasia (6.3%) and Arias stella effect (3.1%).

Simple hyperplasia (36.4%) was the commonest organic cause in the perimenopausal age group followed by complex hyperplasia (24.2%), polyps

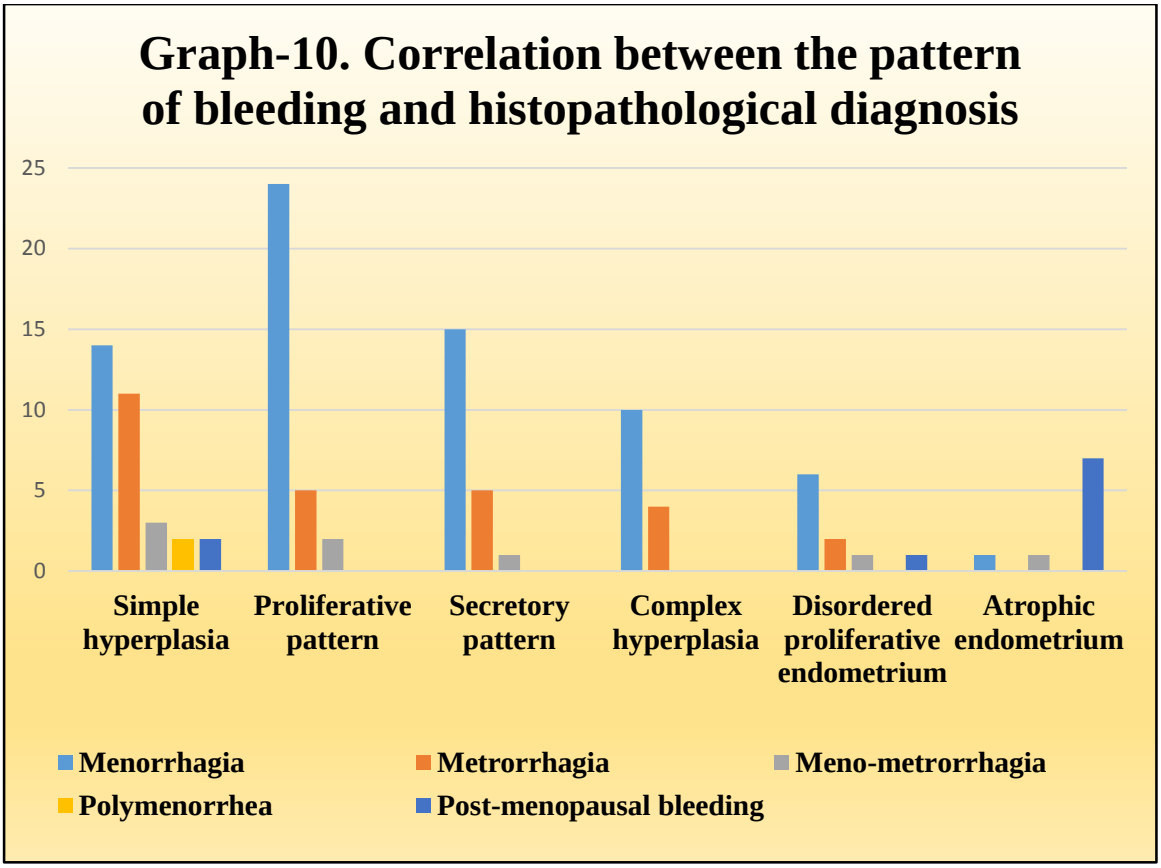
(9.1%), secretory hyperplasia (6.1%), endometrial adenocarcinoma (6.1%), atypical hyperplasia (6.1%), chronic endometritis (6.1%), endometrial metaplasia (3%) and granulomatous TB (3%).

In the post-menopausal age group, there were two cases of simple hyperplasia and one case each in endometrial adenocarcinoma, atypical hyperplasia and squamous cell carcinoma infiltrating endometrium.

Table-10. Correlation between the pattern of bleeding and histopathological diagnosis

Pattern of bleeding	HISTOPATHOLOGICAL DIAGNOSIS	NUMBER OF CASES	%
MR	Proliferative pattern	24	27.3
	Secretory pattern	15	17.0
	Simple hyperplasia	14	15.9
	Complex hyperplasia	10	11.4
	Disordered proliferative endometrium	6	6.8
	Menstrual phase	5	5.7
	Endometrial polyp	5	5.7
	Secretory hyperplasia	2	2.3
	Atypical hyperplasia	2	2.3
	Irregular shedding	1	1.1
	Granulomatous TB	1	1.1
	Endometrial metaplasia	1	1.1
	Atrophic endometrium	1	1.1
	Arias stella effect	1	1.1
	Total	**88**	**100**
MTR	Simple hyperplasia	11	31.4
	Proliferative pattern	5	14.3
	Secretory pattern	5	14.3

	Complex hyperplasia	4	11.4
	Disordered proliferative endometrium	2	5.7
	Secretory hyperplasia	2	5.7
	Endometrial adenocarcinoma	2	5.7
	Endometrial polyp	1	2.9
	Atypical hyperplasia	1	2.9
	Chronic endometritis	1	2.9
	Mixed pattern	1	2.9
	Total	**35**	**100**
MMTR	Simple hyperplasia	3	25.00
	Proliferative pattern	2	16.67
	Secretory pattern	1	8.33
	Disordered proliferative endometrium	1	8.33
	Atrophic endometrium	1	8.33
	Menstrual phase	1	8.33
	Atypical hyperplasia	1	8.33
	Chronic endometritis	1	8.33
	Hormonal changes	1	8.33
	Total	**12**	**100**
PMR	Simple hyperplasia	2	100
	Total	**2**	**100**
PMB	Atrophic endometrium	7	53.8
	Simple hyperplasia	2	15.4
	Disordered proliferative endometrium	1	7.7
	Endometrial adenocarcinoma	1	7.7
	Atypical hyperplasia	1	7.7
	Squamous cell carcinoma infiltrating endometrium	1	7.7
	Total	**13**	**100**

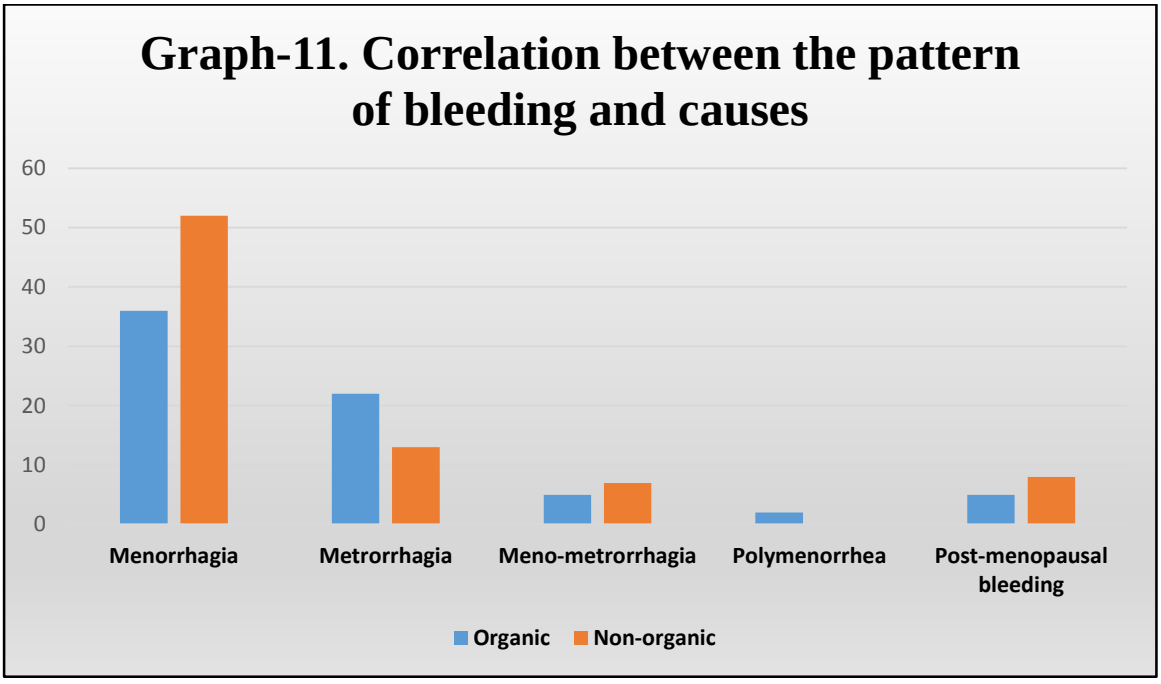


The histological diagnosis in patients presenting with menorrhagia in decreasing order of frequency are proliferative pattern (27.3%), secretory pattern (17%), simple hyperplasia (15.9%) , complex hyperplasia (11.4%), disordered proliferative endometrium (6.8%), endometrial polyp (5.7%), menstrual phase endometrium (5.7%) and so on.

The histological findings in patients presenting with metrorrhagia are simple hyperplasia (31.4%), proliferative pattern (14.3%), secretory pattern (14.3%), complex hyperplasia (11.4%), disordered proliferative endometrium (5.7%), secretory hyperplasia (5.7%), endometrial adenocarcinoma (5.7%) and so on.

Table-11. Correlation between the pattern of bleeding and causes

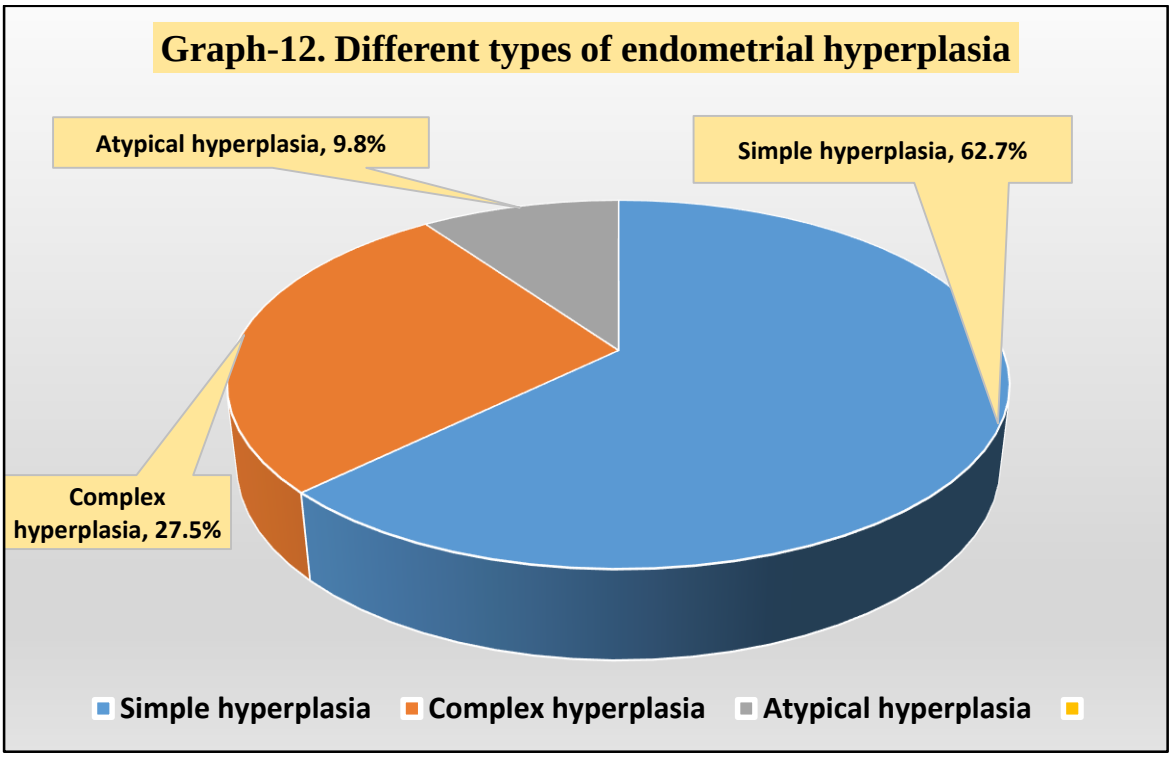
S.№	Pattern of bleeding	Organic	Non-organic
1	Menorrhagia	36	52
2	Metrorrhagia	22	13
3	Meno-metrorrhagia	5	7
4	Polymenorrhea	2	0
5	Post-menopausal bleeding	5	8
	Total	70	80



In abnormal uterine bleeding due to both organic and non-organic causes, menorrhagia was the commonest pattern of bleeding followed by metrorrhagia.

Table-12. Different types of endometrial hyperplasia

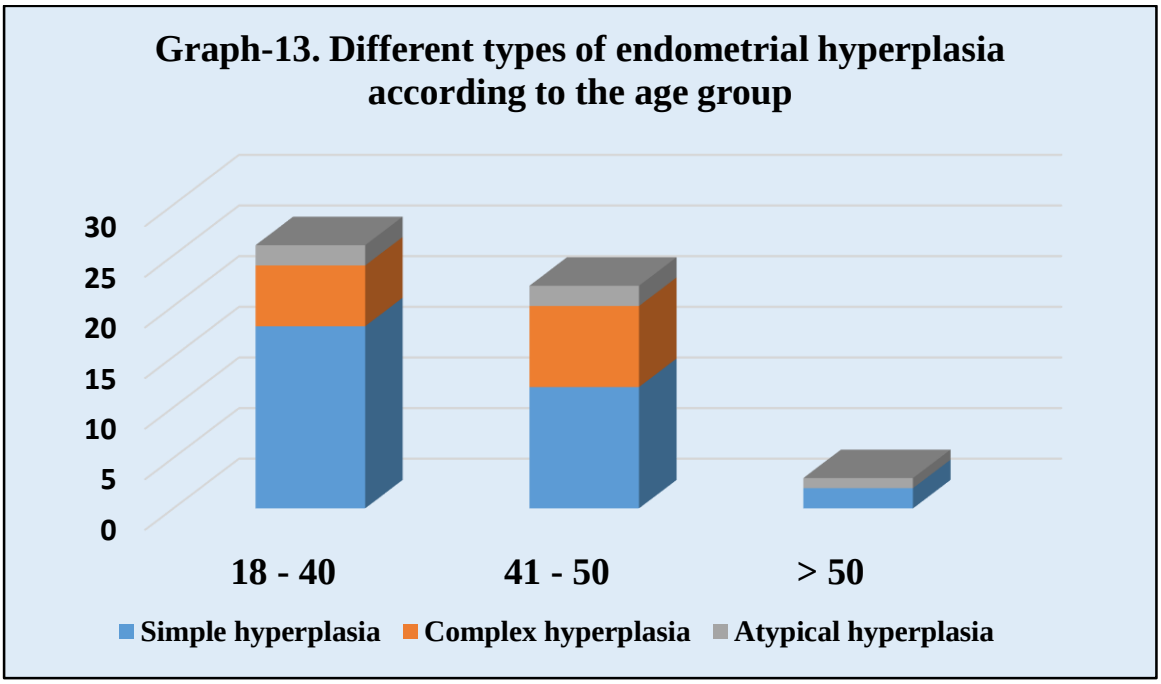
S.№	Type	№ of cases	%
1	Simple hyperplasia	32	62.7
2	Complex hyperplasia	14	27.5
3	Atypical hyperplasia	5	9.8
	Total	51	100



Among the various types of hyperplasias (total= 51), simple hyperplasia (62.7%) was the commonest type followed by complex hyperplasia (27.5%) and atypical hyperplasia (9.8%).

Table-13. Different types of endometrial hyperplasia according to the age group

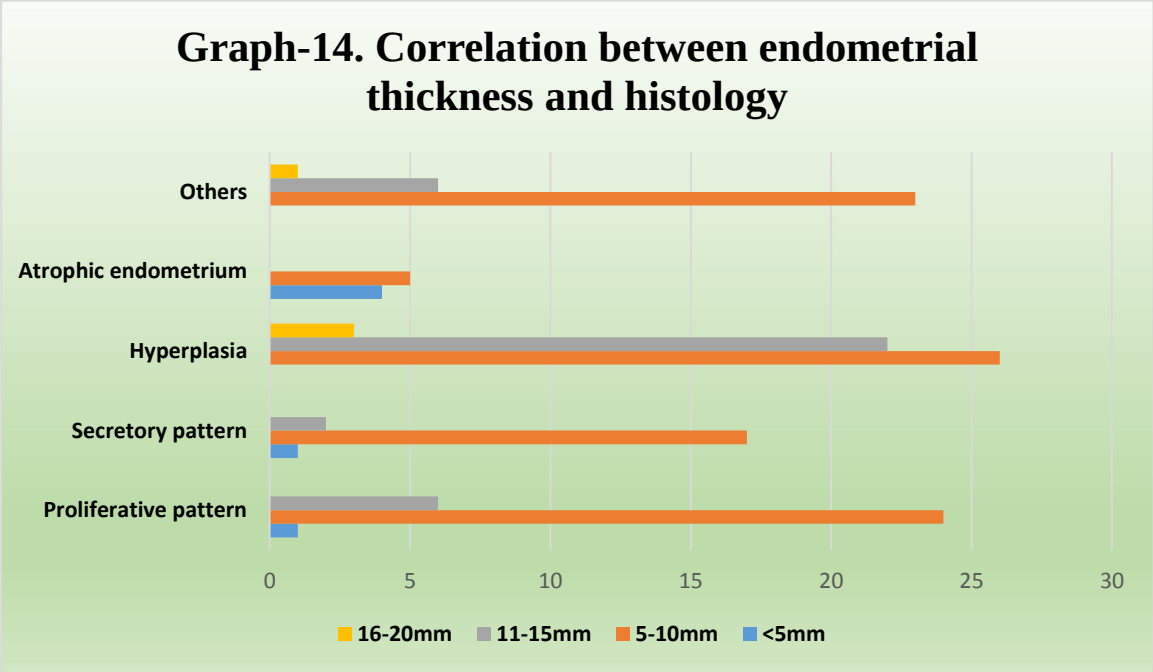
S.№	Type	18 - 40	41 - 50	> 50	Total	%
1	Simple hyperplasia	18	12	2	32	62.7
2	Complex hyperplasia	6	8	0	14	27.5
3	Atypical hyperplasia	2	2	1	5	9.8
	Total	26	22	3	51	100



Age-wise analysis of the distribution of hyperplasias revealed that simple hyperplasia was the commonest type of hyperplasia seen in all the three age groups followed by complex hyperplasia and atypical hyperplasia.

Table-14. Correlation between endometrial thickness and histology

S.№	Histology	Endometrial thickness (mm)				Total
		<5	5-10	11-15	16-20	
1	Proliferative pattern	1	24	6	0	31
2	Secretory pattern	1	17	2	0	20
3	Hyperplasia	0	26	22	3	51
4	Atrophic endometrium	4	5	0	0	9
5	Others	0	23	6	1	30
	Total	6	95	36	4	141



Correlation between endometrial thickness and the histological pattern revealed that most cases of hyperplasia have an endometrial thickness between 5 and 15 mm (with 3 case having a thickness > 15 mm), whereas all cases of atrophic endometrium have endometrial thickness < 10 mm. Thus the histological diagnosis correlated well with the ultrasound findings.

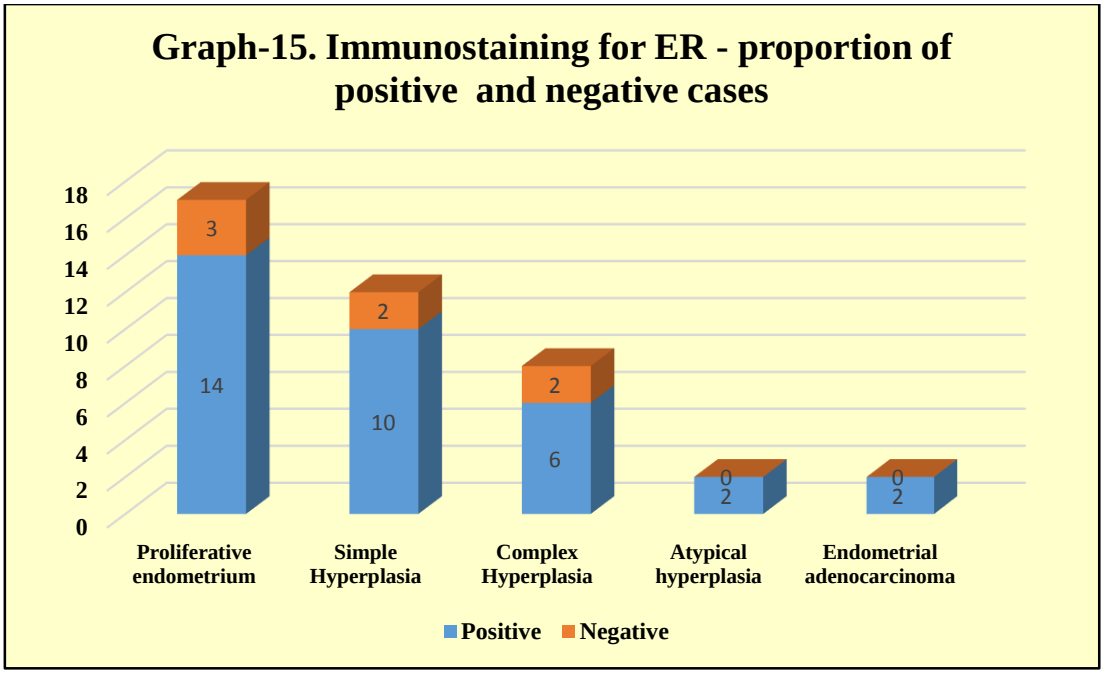
Table-15. Immunohistochemical staining of ER and PR in the glandular epithelium of perimenopausal women presenting with AUB

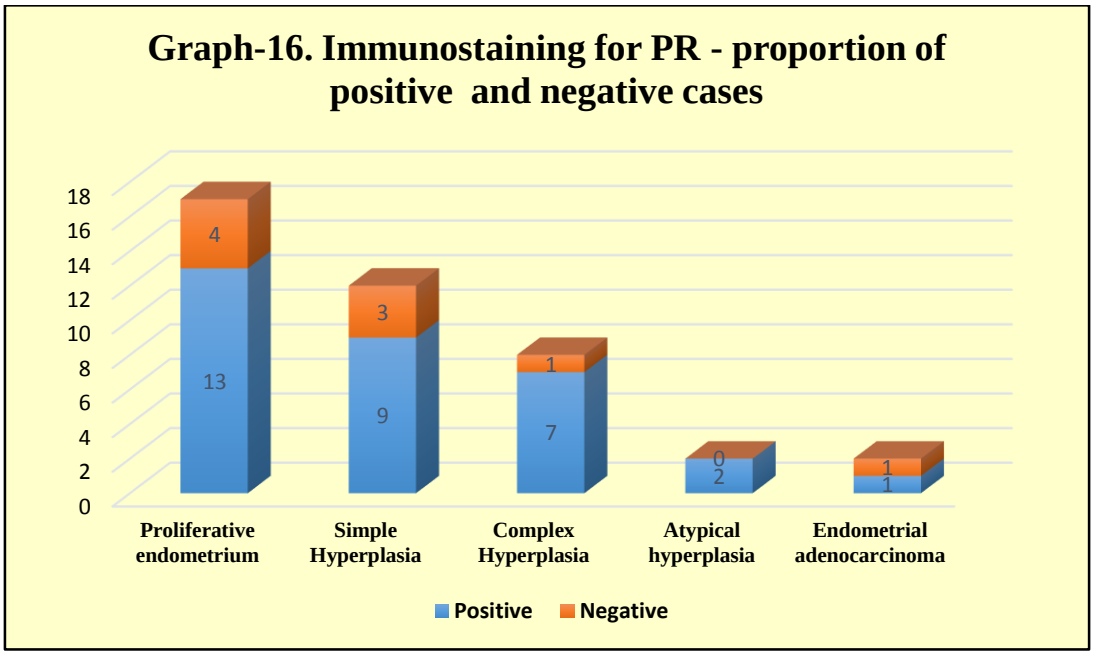
Immunostaining	**ER**				**PR**			
Endometrial changes	**Positive**		**Negative**		**Positive**		**Negative**	
	N	%	N	%	N	%	N	%
Non-malignant	32	94.1	7	100	31	96.9	8	88.9
Malignant	2	5.9	0	0	1	3.1	1	11.1
Total	34	100	7	100	32	100	9	100

Immunohistochemical staining was done in perimenopausal women with histological diagnosis of proliferative endometrium, all types of hyperplasia and endometrial adenocarcinoma. Analysis of the results of immunostaining revealed that both the cases of endometrial adenocarcinoma were positive for both ER and PR, whereas in the remaining 39 cases of non-malignant endometrium 32 (94.1%) cases were positive for ER and 31 (96.9%) cases were positive for PR.

Table-16. Correlation between immunostaining for ER, PR and histopathological findings

Immunostaining	**ER**		**PR**	
Histopathologic finding	**N**	**% of positive cases**	**N**	**% of positive cases**
Proliferative endometrium	14/17	82.35	13/17	76.47
Simple Hyperplasia	10/12	83.33	9/12	75.00
Complex Hyperplasia	6/8	75.00	7/8	87.50
Atypical hyperplasia	2/2	100.00	2/2	100.00
Endometrial adenocarcinoma	2/2	100.00	1/2	50.00
Total	33/41	80.49	32/41	78.05



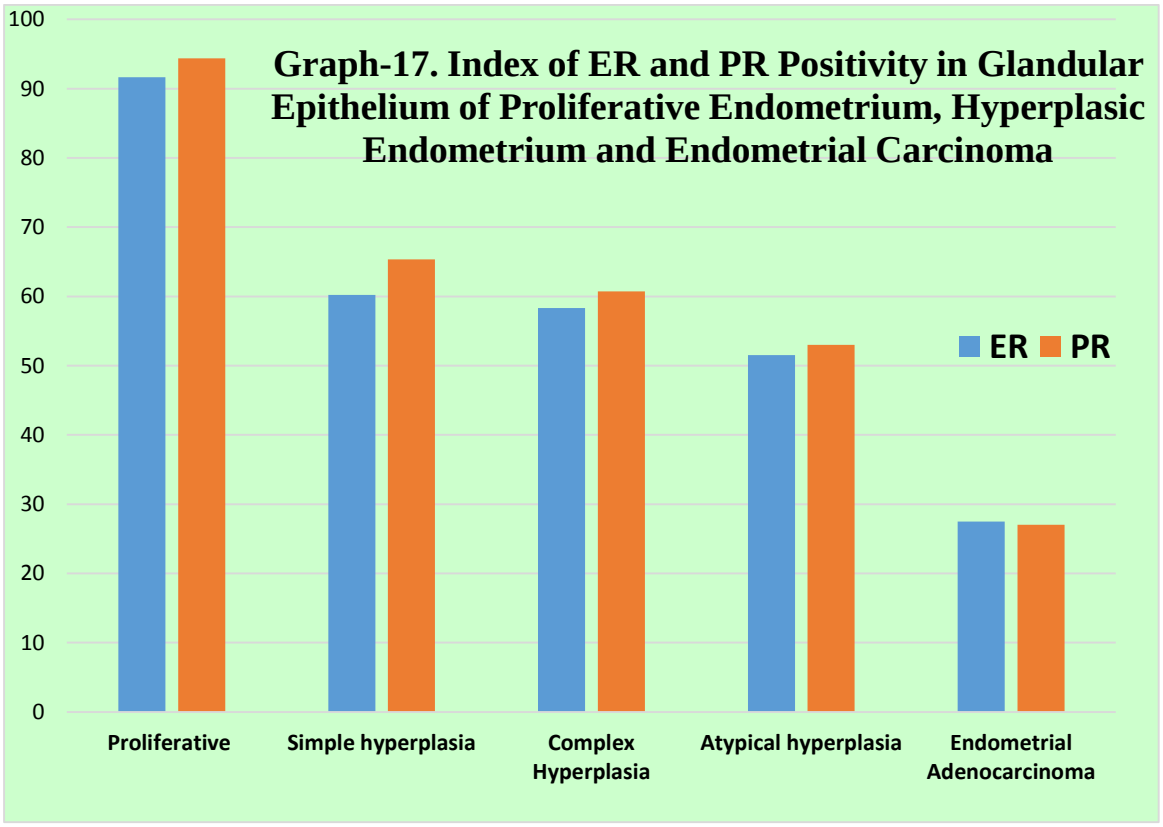


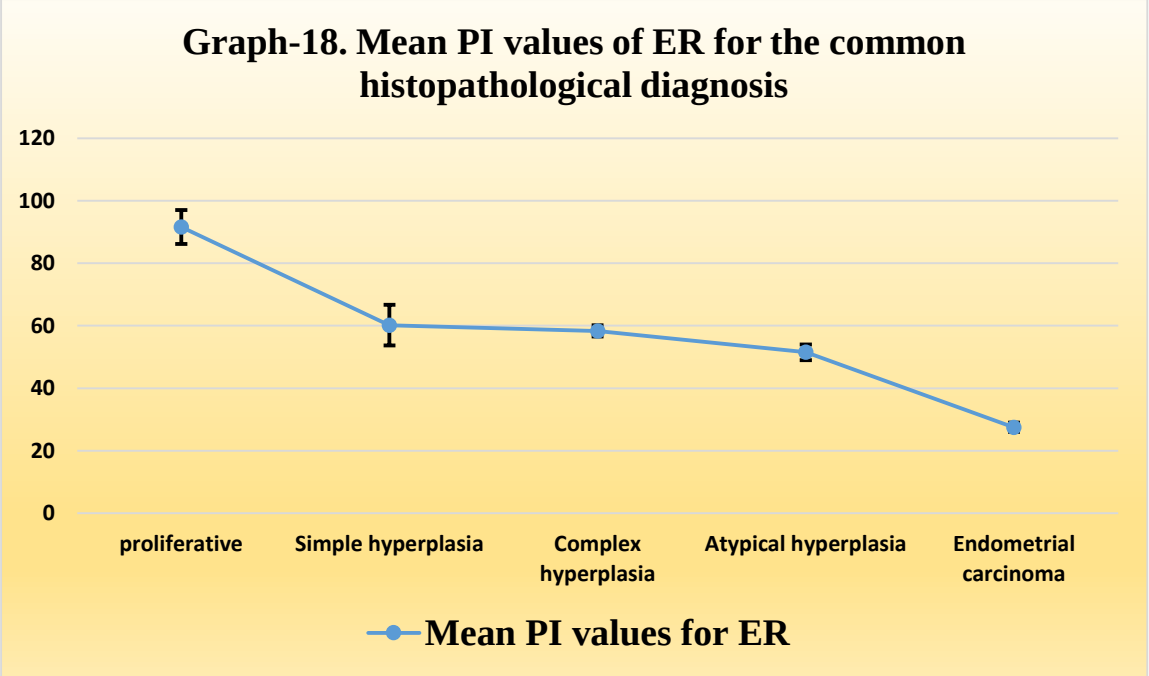
All cases of atypical hyperplasia and endometrial carcinoma were positive for both ER and PR. Among proliferative endometrium, 82.35% were positive for ER and 76.47% were positive for PR. In simple hyperplasia, the percentage of cases showing positivity for ER and PR are respectively 83.33% and 75%. In complex hyperplasia, the percentage of cases positive for ER and PR are respectively 75% and 87.5%.

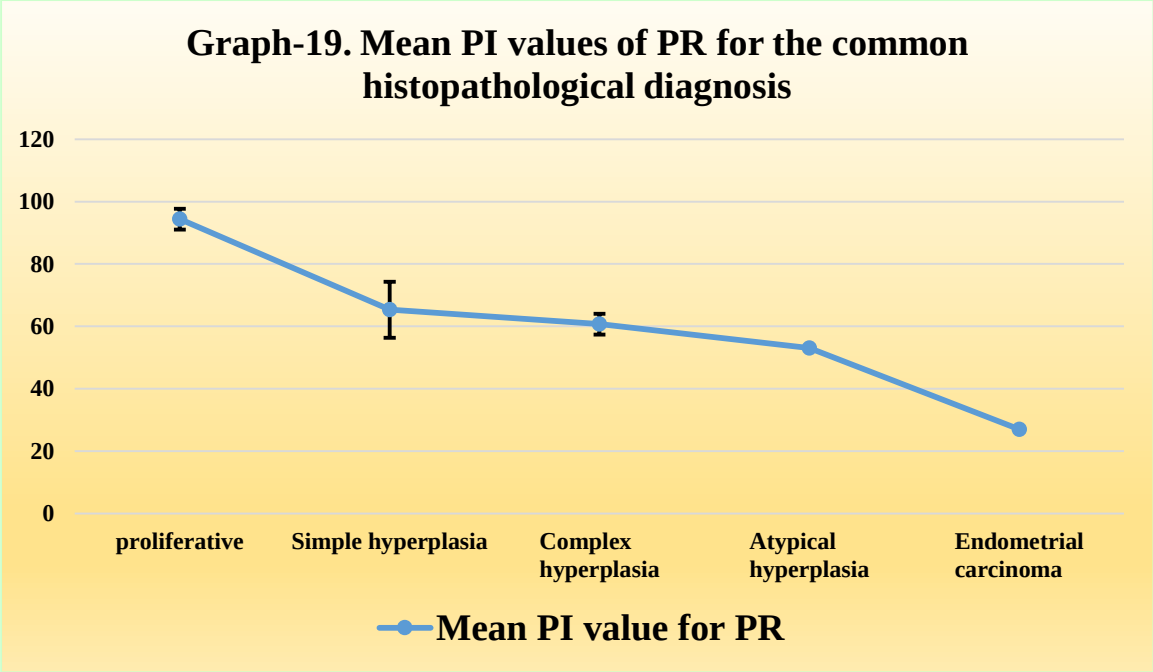
Table-17. Index of ER and PR Positivity in Glandular Epithelium of Proliferative Endometrium, Hyperplasic Endometrium and Endometrial Carcinoma

S.№	Histopathological diagnosis	ER			PR		
		N	PI-ER %	P	N	PI- PR %	P
1	Proliferative	14	91.64	<0.001	13	94.38	<0.001
2	Simple hyperplasia	10	60.20		9	65.33	
3	Complex Hyperplasia	6	58.33		7	60.71	
4	Atypical hyperplasia	2	51.50		2	53.00	
5	Endometrial Adenocarcinoma	2	27.50		1	27.00	

* **PI**- percentage index







The analysis of the percentage of positively stained cells was done by counting the number of positively stained cells divided by the total number of cells counted. The percentages were calculated for each case and the mean of the percentages calculated for all cases in each category of diagnosis. It is observed

that mean PI values to ER were highest for proliferative endometrium (91.64%) followed by simple hyperplasia (60.20%), complex hyperplasia (58.33%), atypical hyperplasia (51.5%) and endometrial carcinoma (27%). Similar findings were seen with respect to mean PI values to PR positivity with the highest values for proliferative pattern (94.38%) and lowest mean PI value for endometrial carcinoma (27%).

One-way analysis of variance is used to determine whether there are any significant differences between the mean PI values for ER and PR of the three common categories that is the proliferative pattern, simple hyperplasia and complex hyperplasia. Atypical hyperplasia and endometrial carcinoma were not included in the analysis because of small sample size. The statistical analysis revealed that the differences between the mean PI values of the three common categories are highly significant ($p < 0.001$).

FIGURES

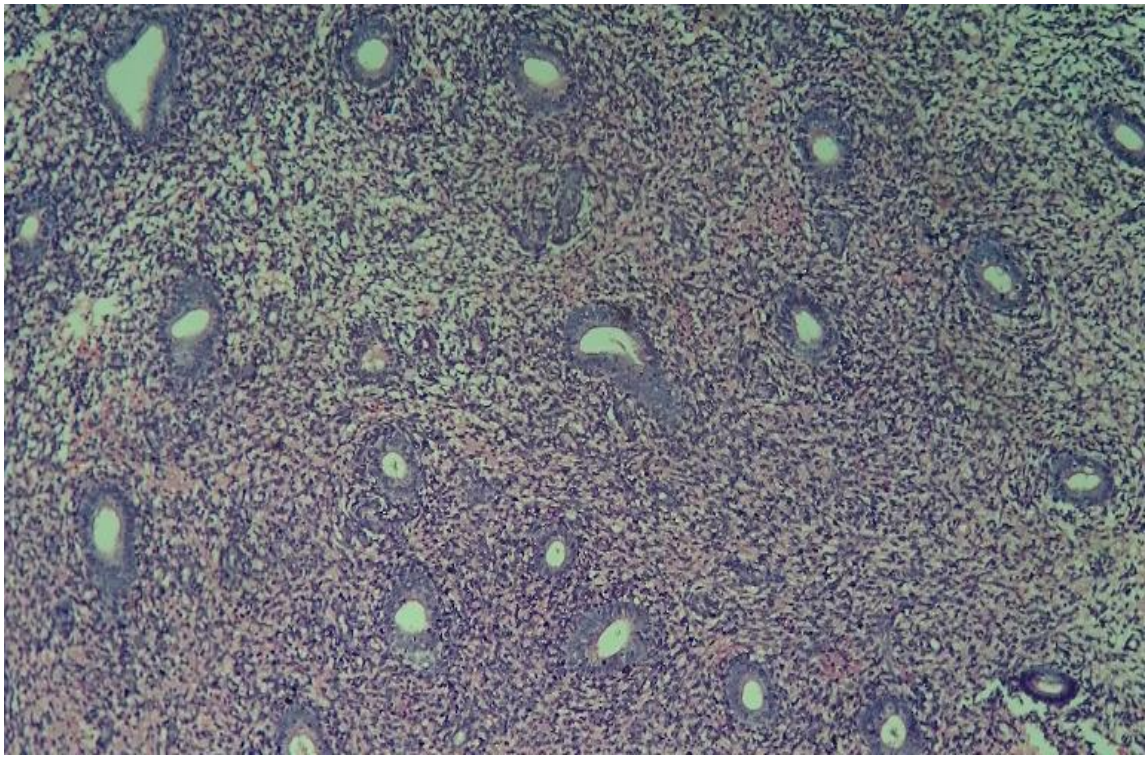


Figure-1A. Proliferative Pattern 10x magnification

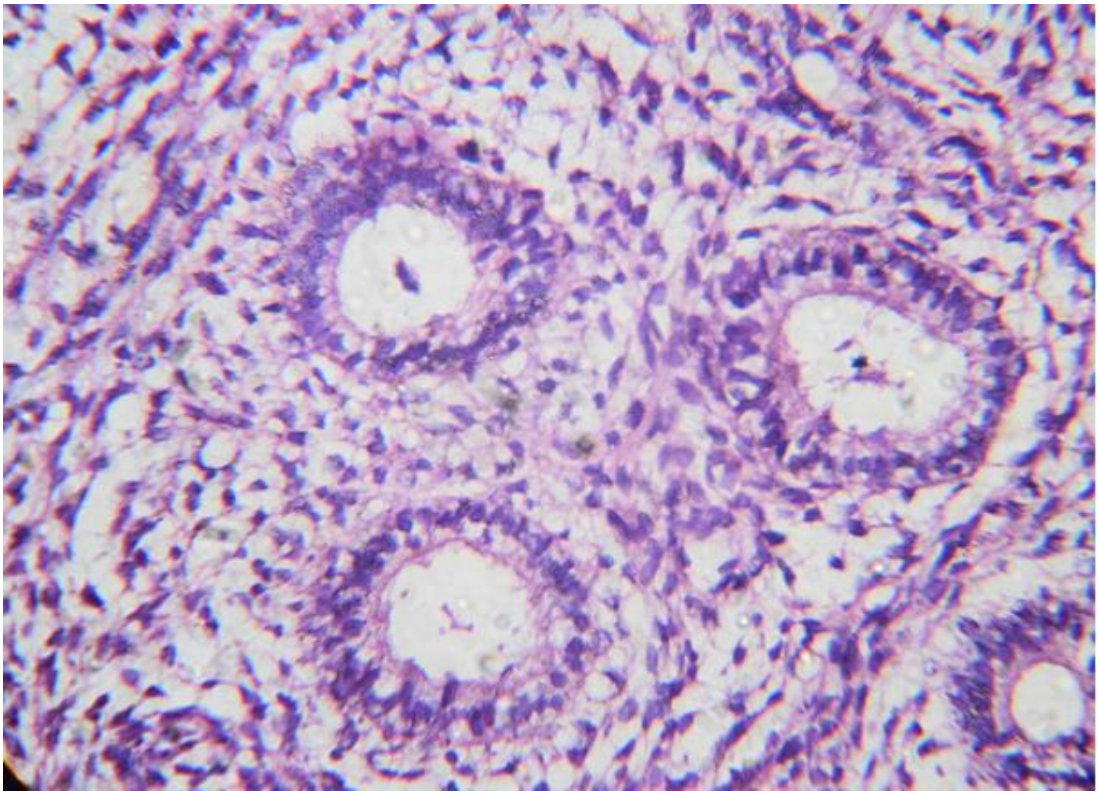


Figure-1B. Proliferative Pattern photomicrograph 40x magnification showing widely spaced tubular glands, pseudostratification and mitosis

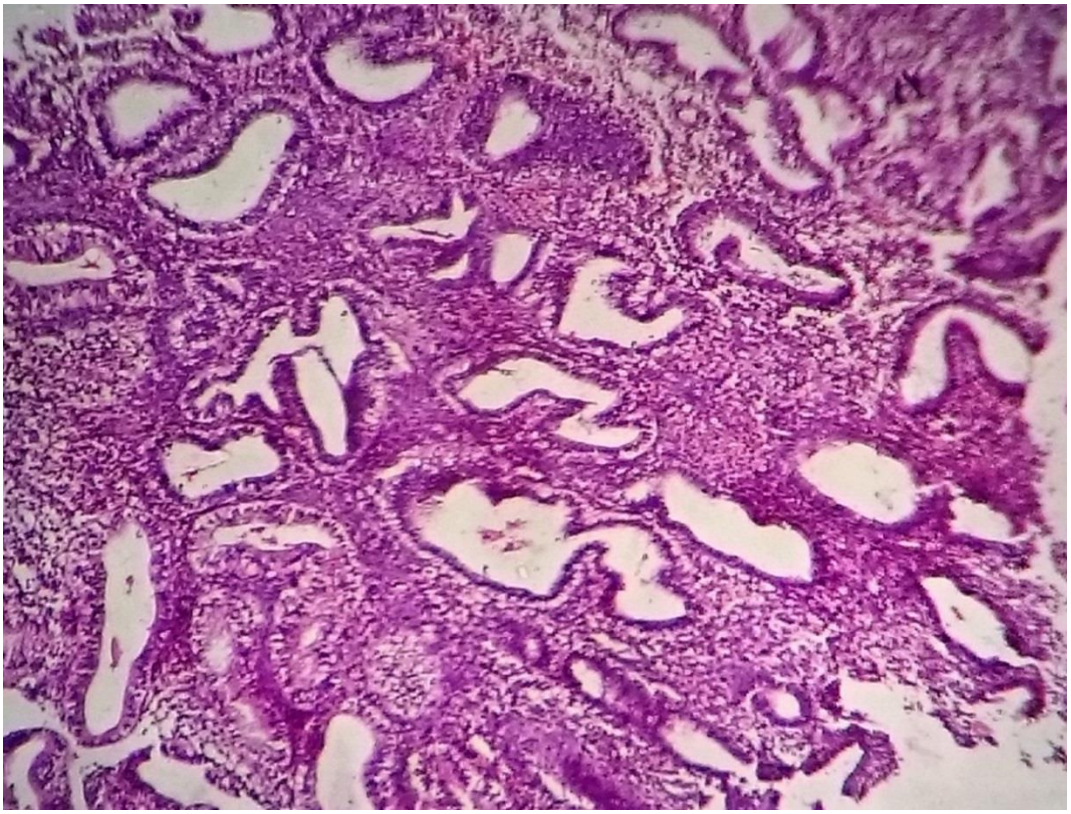


Figure-2A Secretory phase scanner view to show tortuosity of glands.

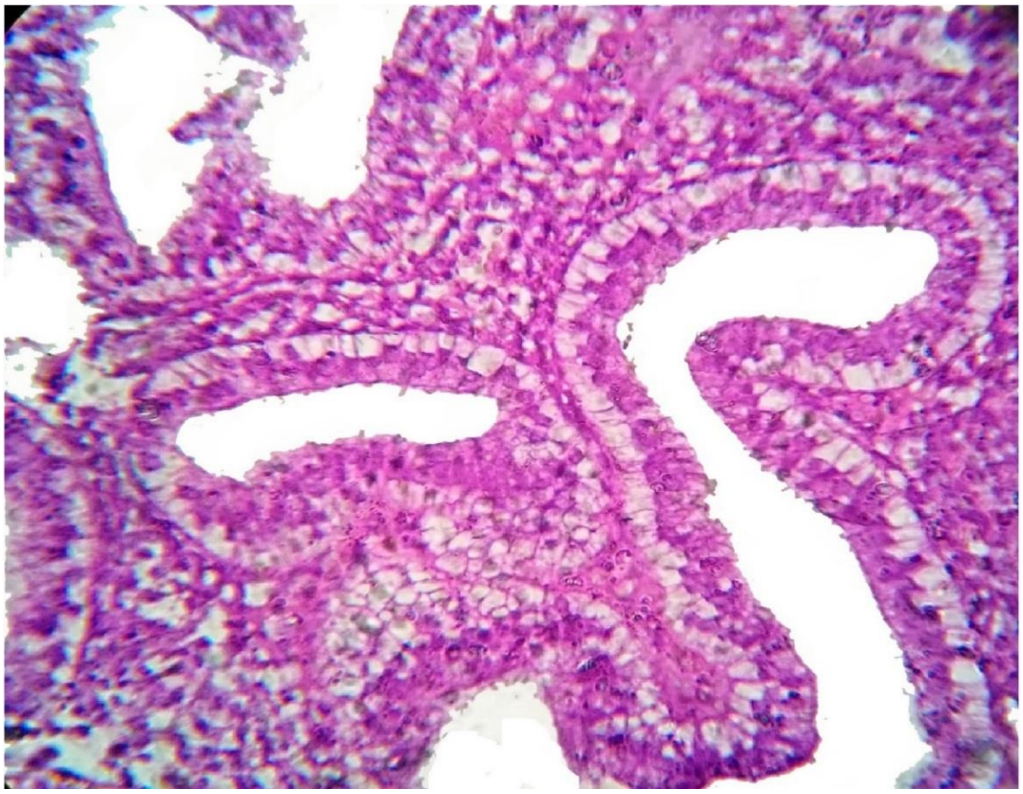


Figure-2B. Secretory phase-photomicrograph under 40x showing tubular glands with subnuclear vacuolation.

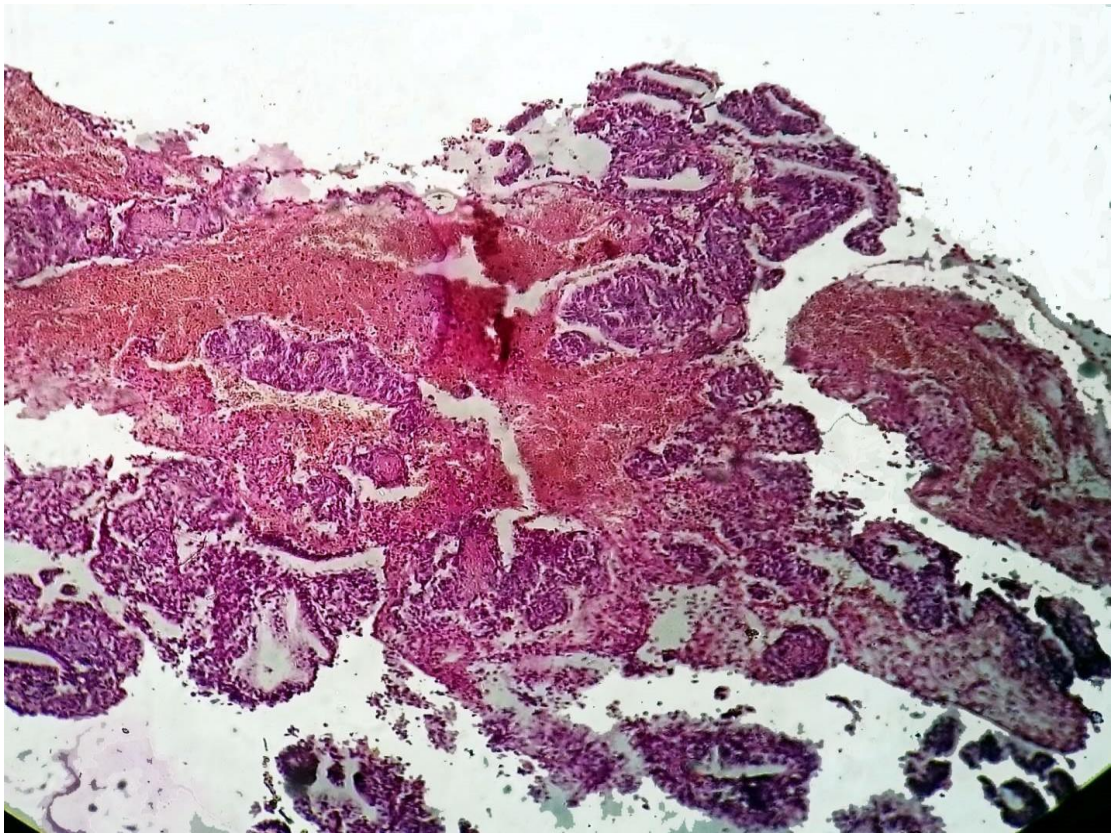


Figure-3. Menstrual phase photomicrograph under 10x magnification showing broken endometrial glands and haemorrhage

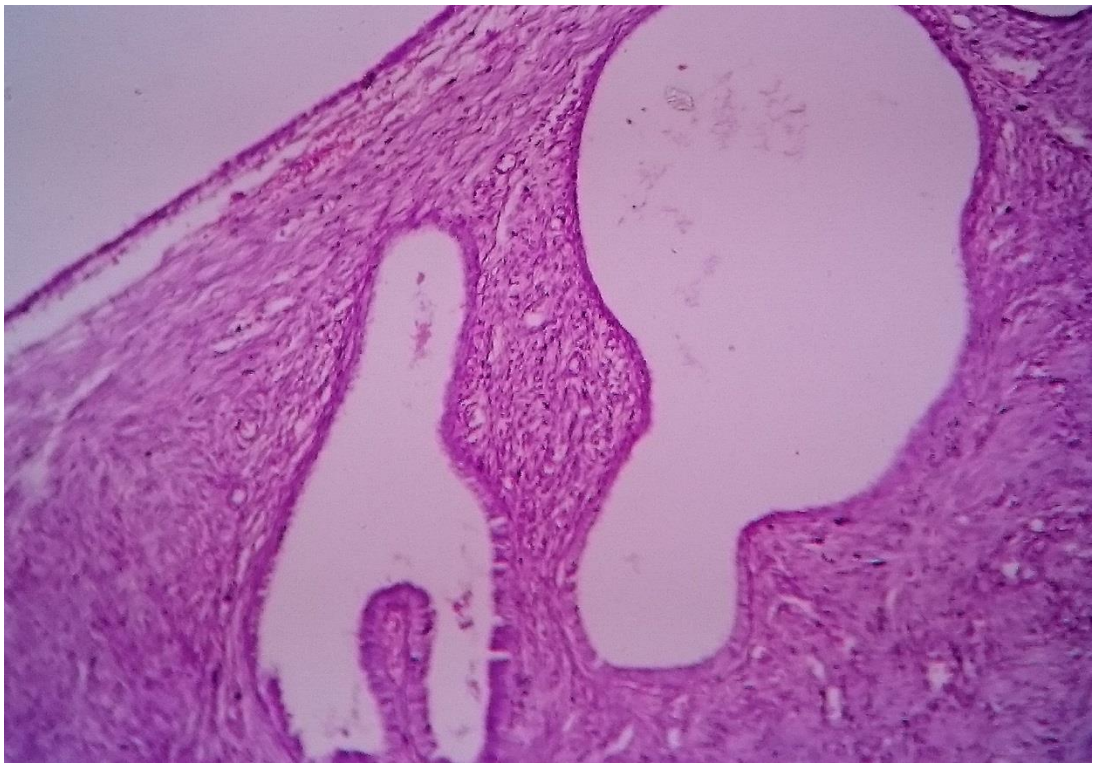


Figure-4. Atrophic endometrium

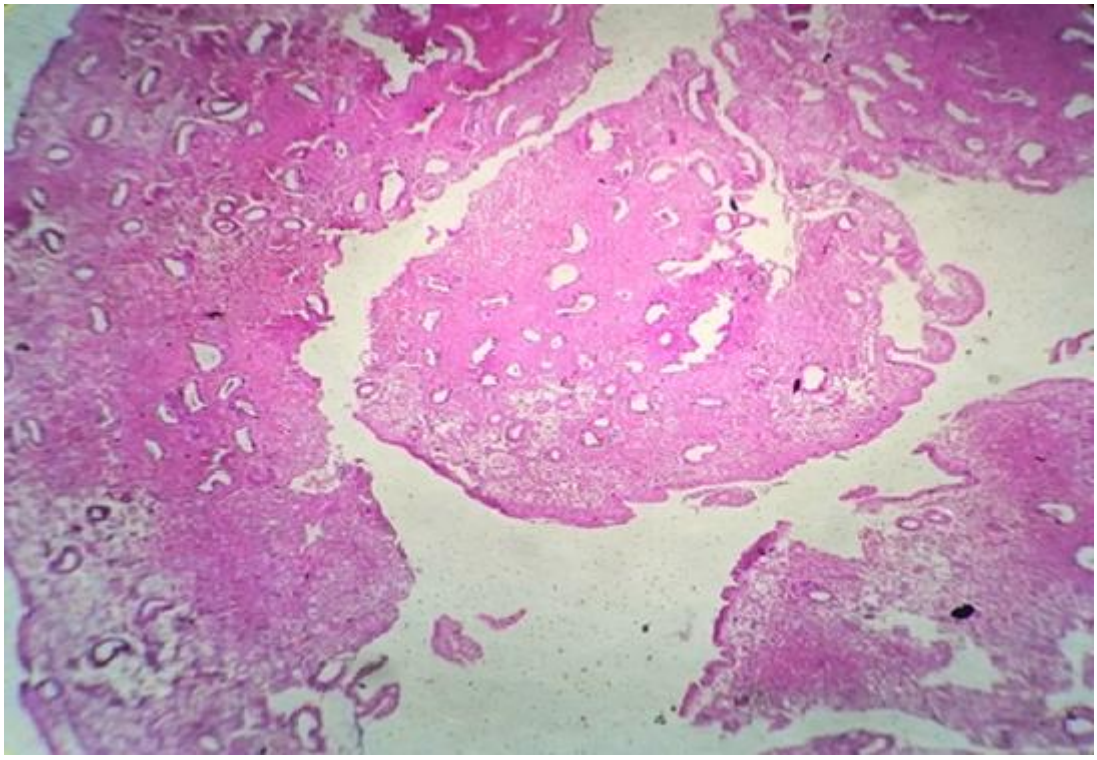


Figure-5A. Polyp -photomicrograph under the scanner shows polypoidal fragments with lining epithelium, focal glandular dilation and crowding and thick walled blood vessels.

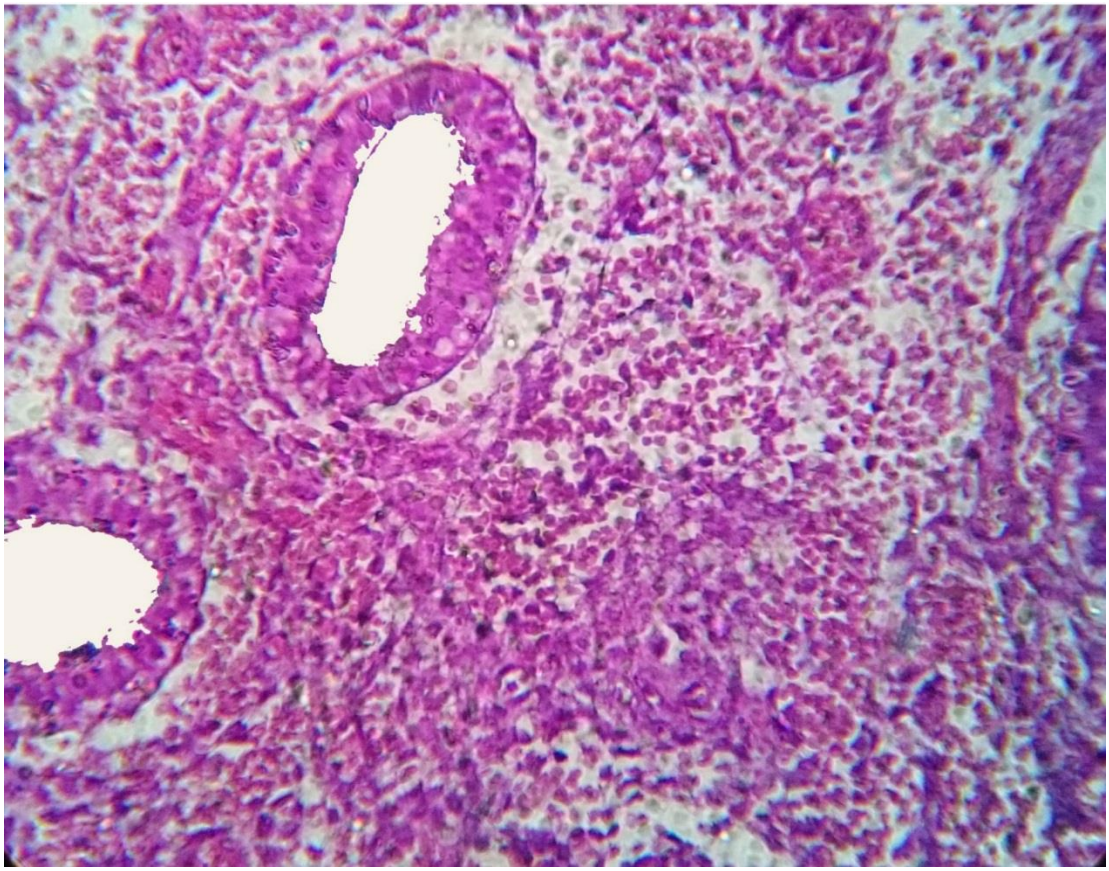


Figure-5B. Polyp -under 40x magnification thick walled blood vessels

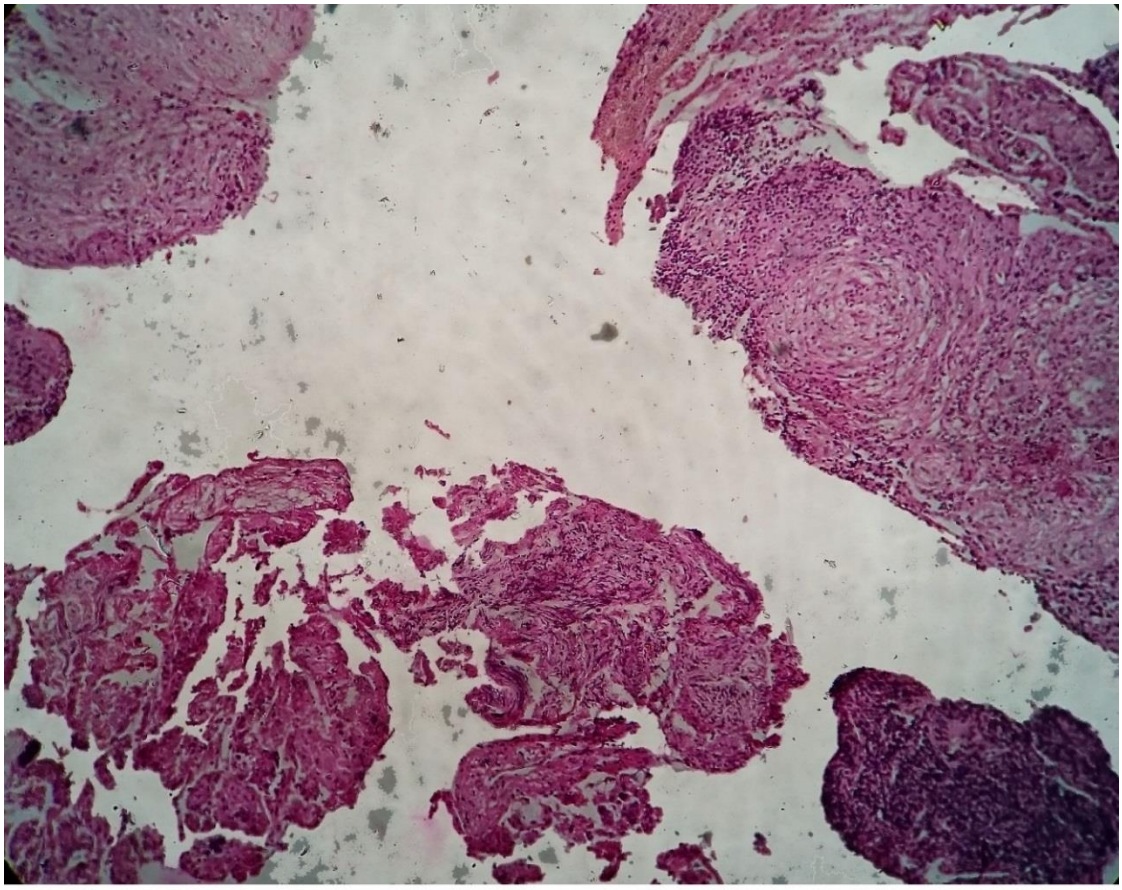


Figure-6A. Granulomatous TB scanner view, showing granulomas composed of giant cells, epitheloid cell and necrosis.

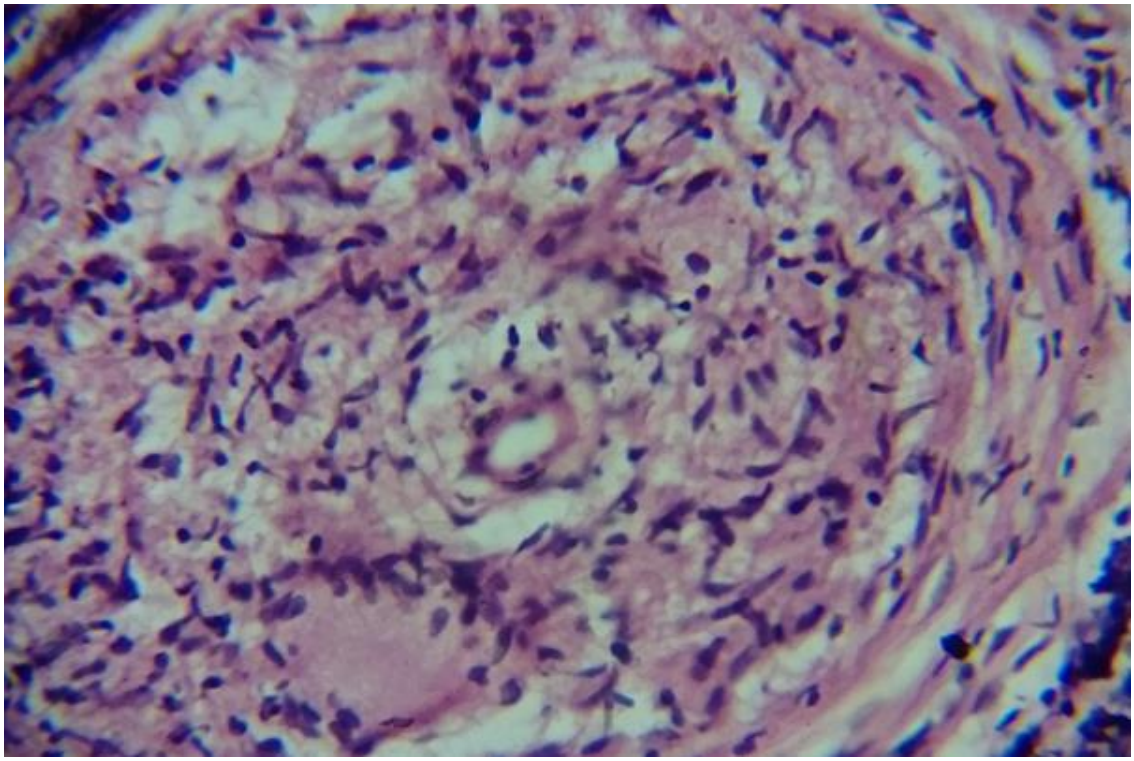


Figure-6B. Granulomatous TB 40 x showing –granuloma with the typical langhans giant cell.

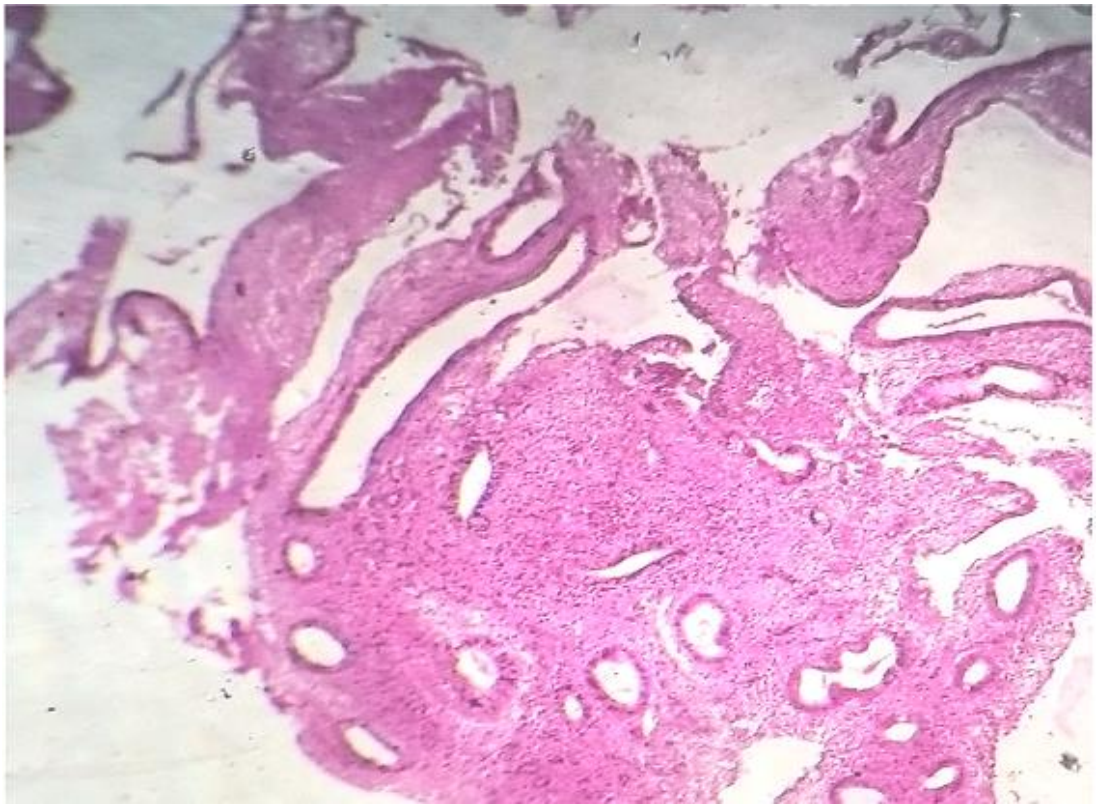


Figure-7. DOP photomicrograph showing occasional cystically dilated glands admixed with short tubular glands.

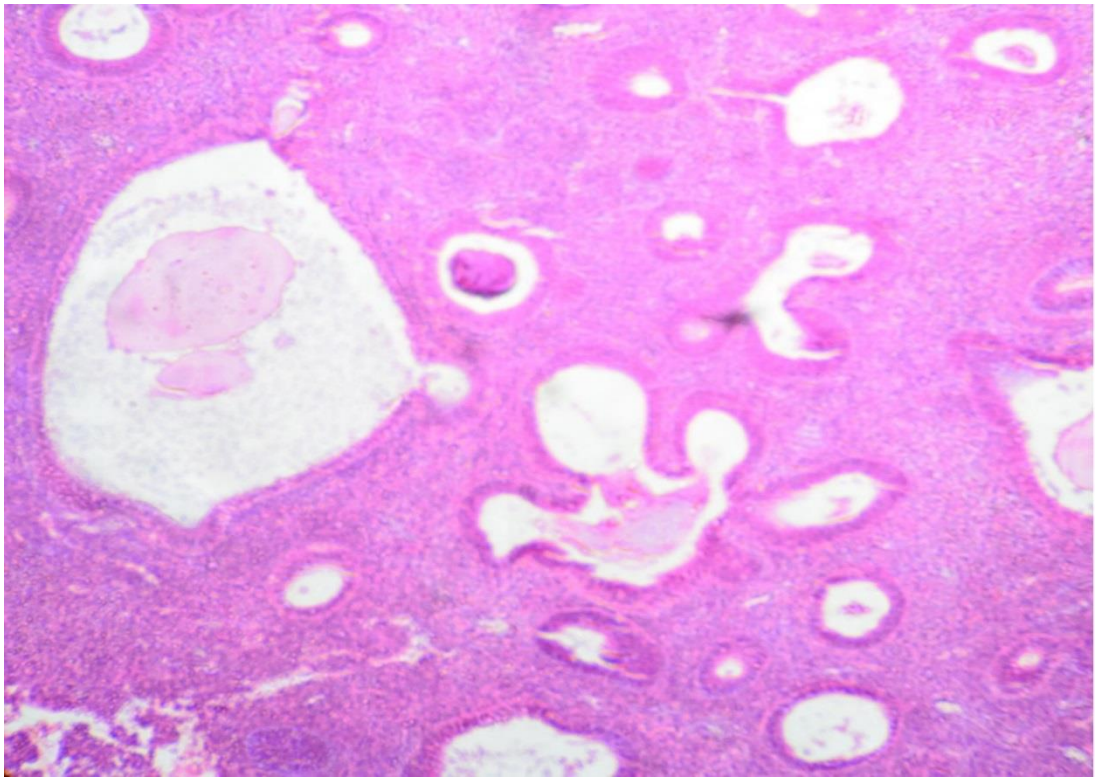


Figure-8. Simple Hyperplasia under 40 x magnification showing minimally crowded glands with outpouchings.

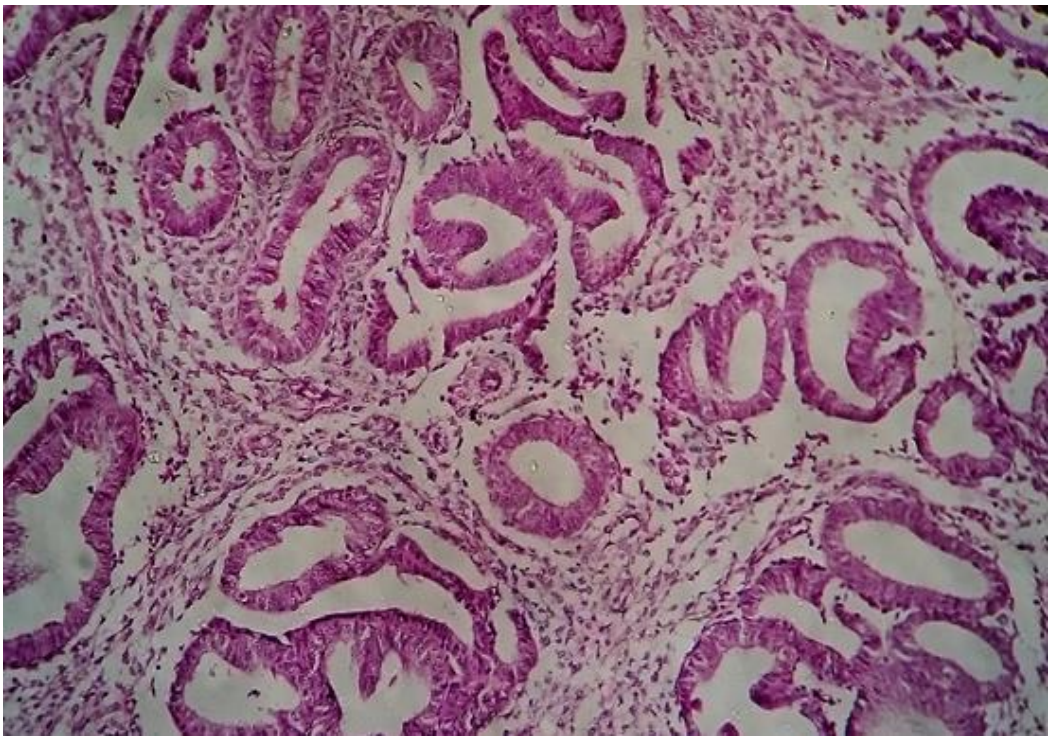


Figure-9. Complex Hyperplasia without atypia-back to back glands with complex branching infoldings and minimal intervening stroma

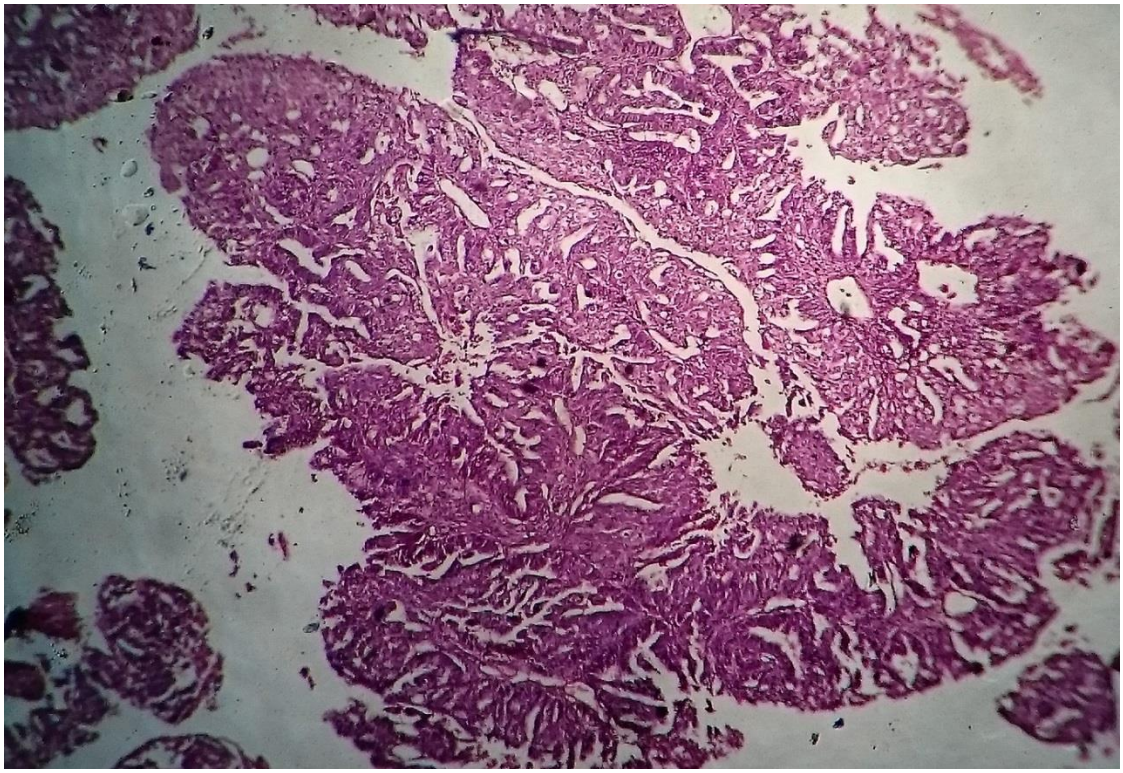


Figure-10A. Scanner showing complex hyperplasia with atypia.

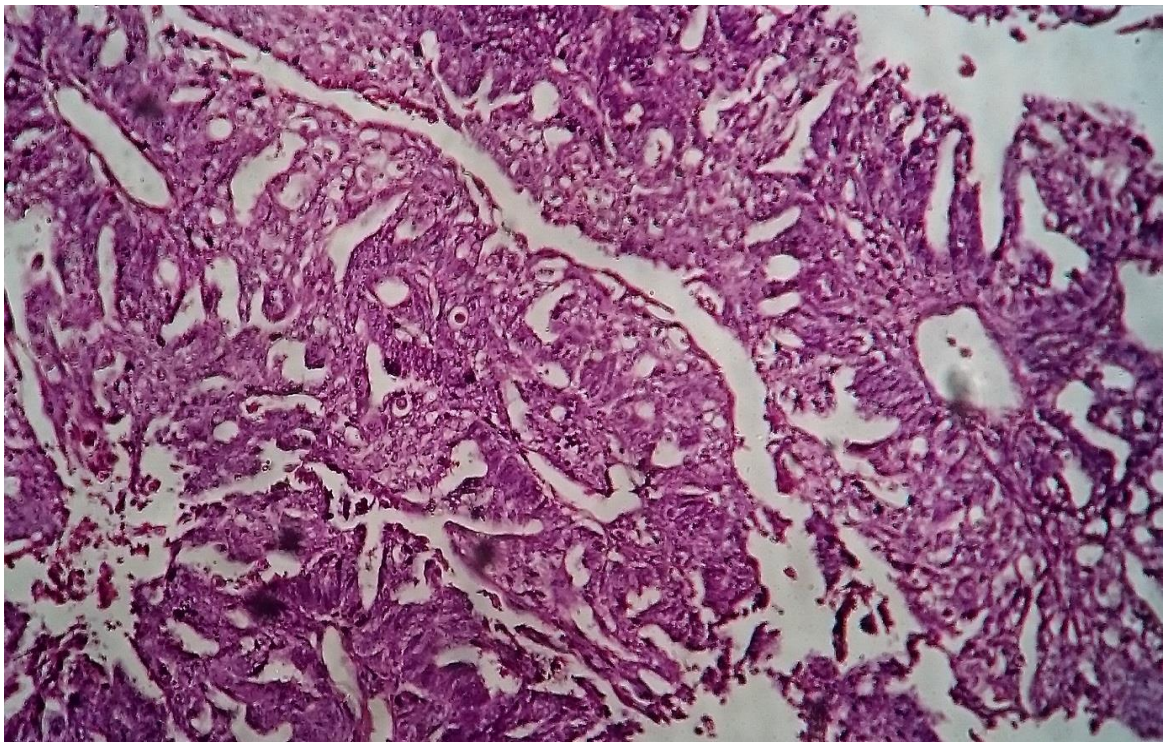


Figure-10B. Complex hyperplasia with atypia 10x magnification glands are back to back with complex branching and nuclear atypia.

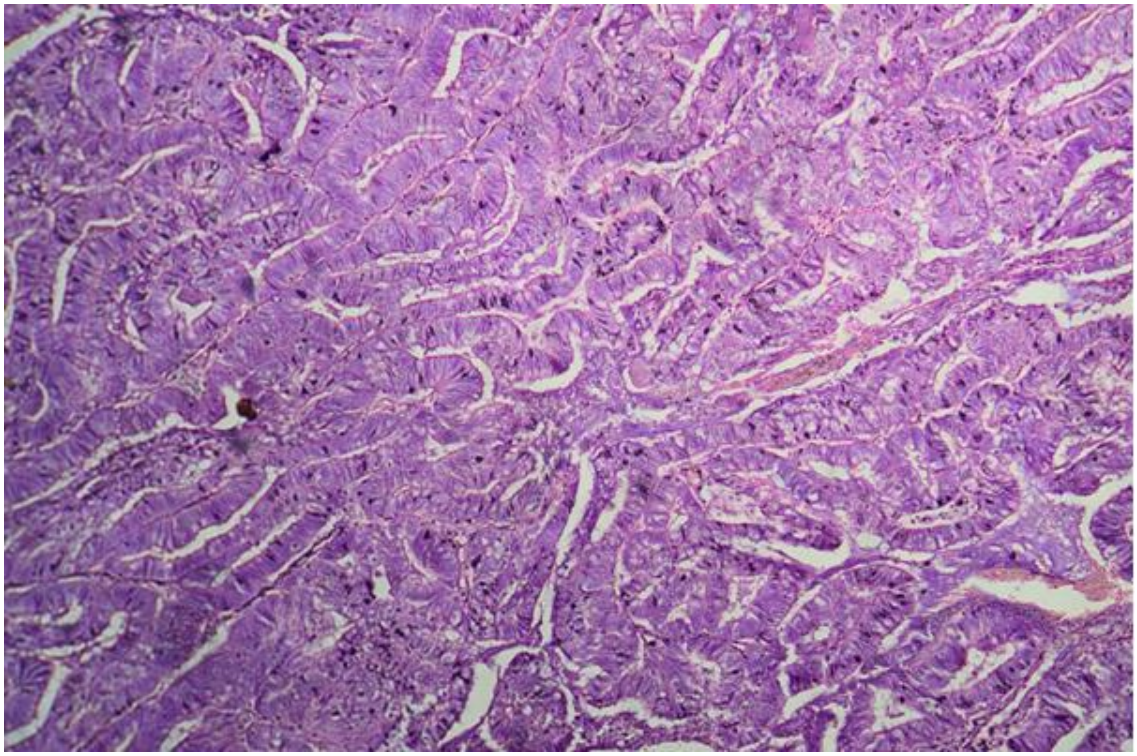


Figure-11. Adenocarcinoma-40x magnification complex branching forming labyrinthine pattern with no intervening stroma.

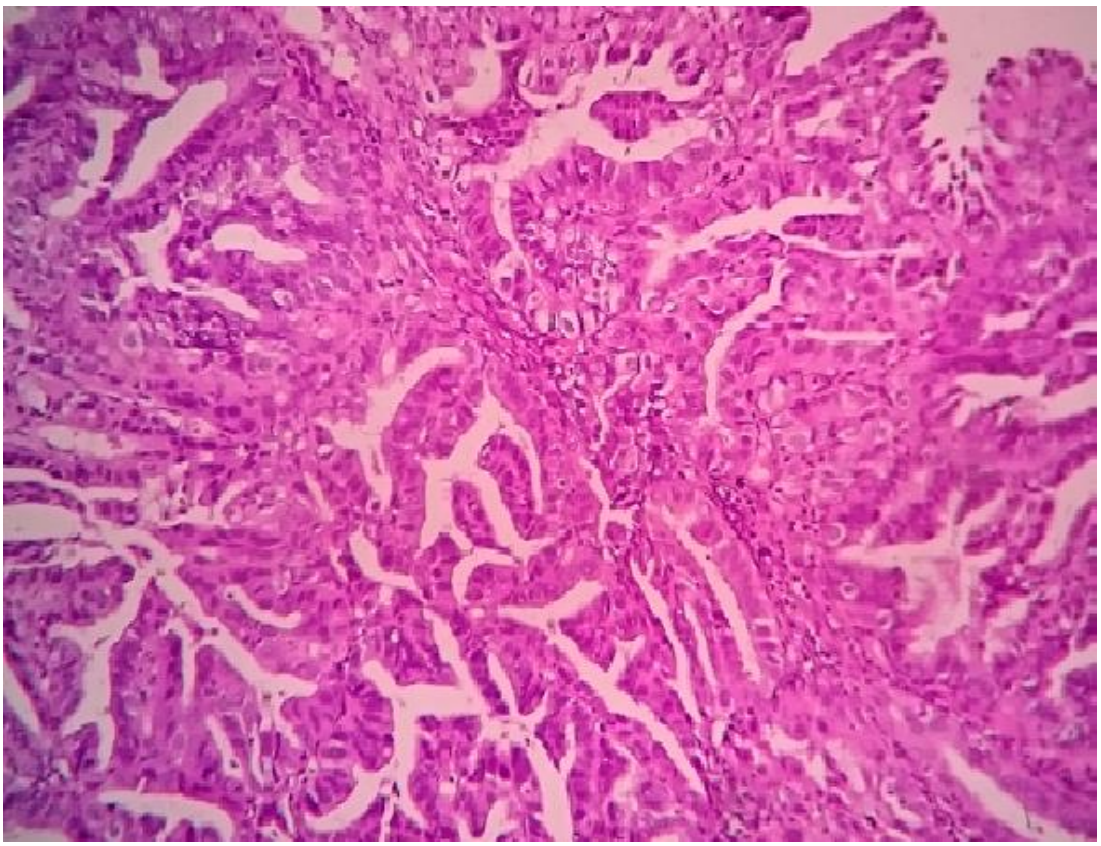


Figure-12. Endometrial adenocarcinoma – villoglandular pattern

MIMICKERS OF PRE-MALIGNANT AND MALIGNANT LESIONS

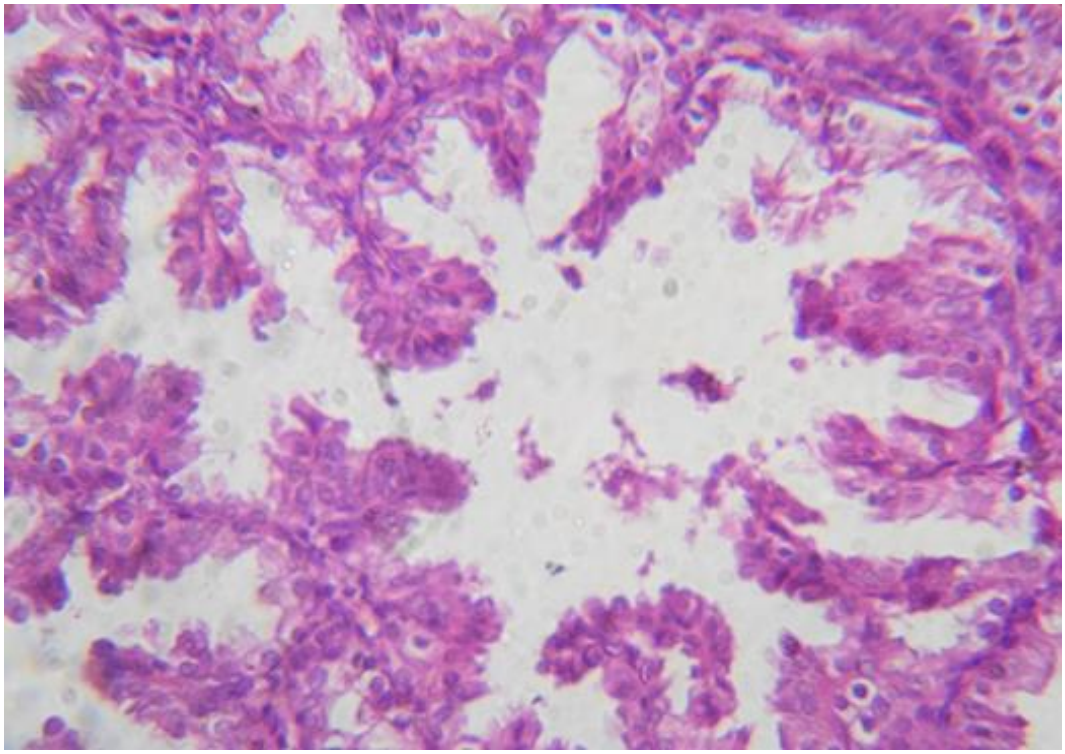


Figure-13. Arias Stella Reaction

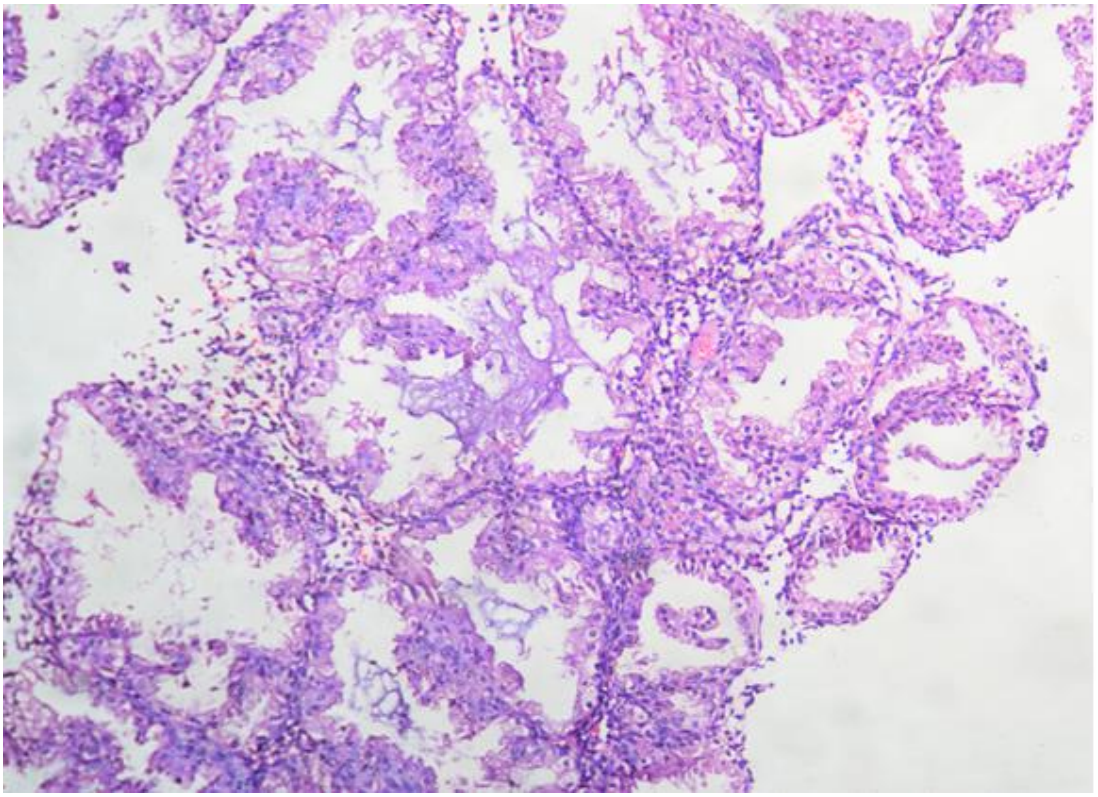


Figure-14. Secretory Exhaustion

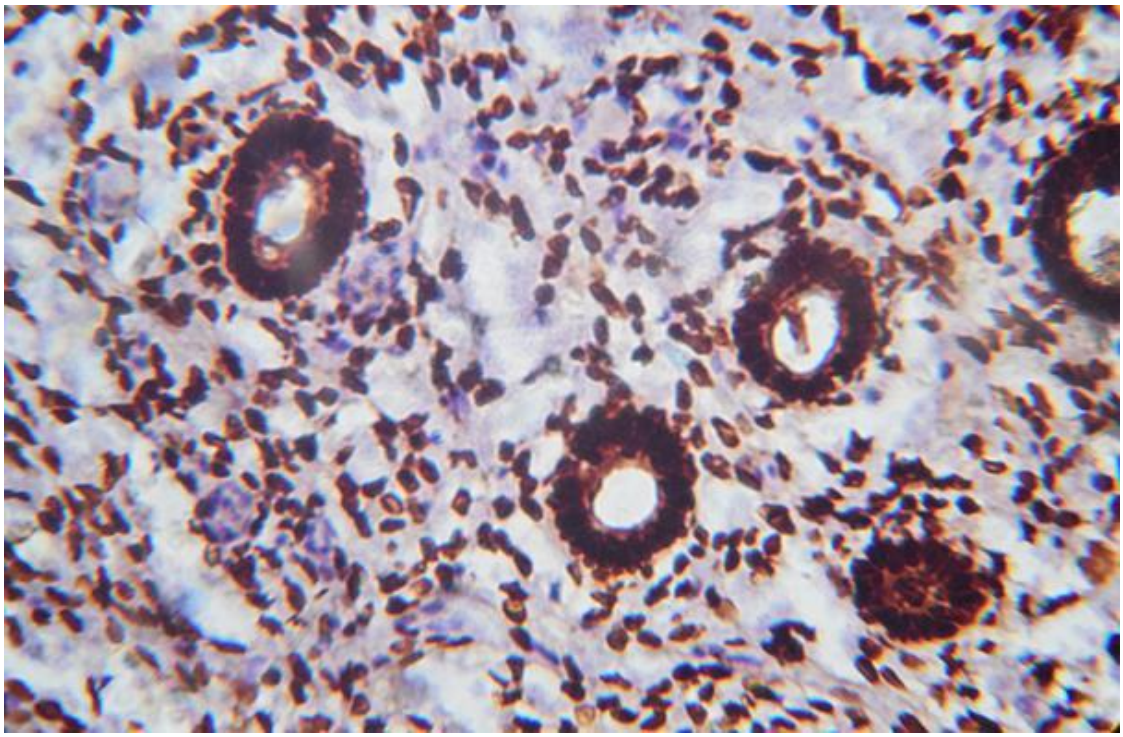


Figure-15. ER of proliferative endometrium-40x magnification strong and intense nuclear positivity.

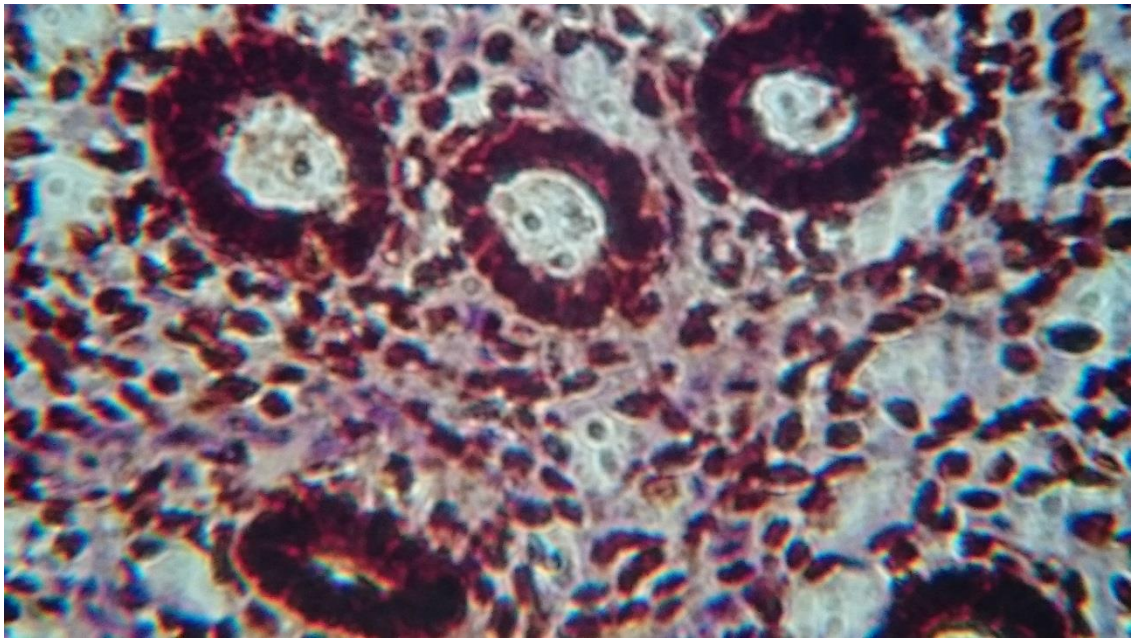


Figure-16. PR of proliferative endometrium-40x magnification strong and intense nuclear positivity.

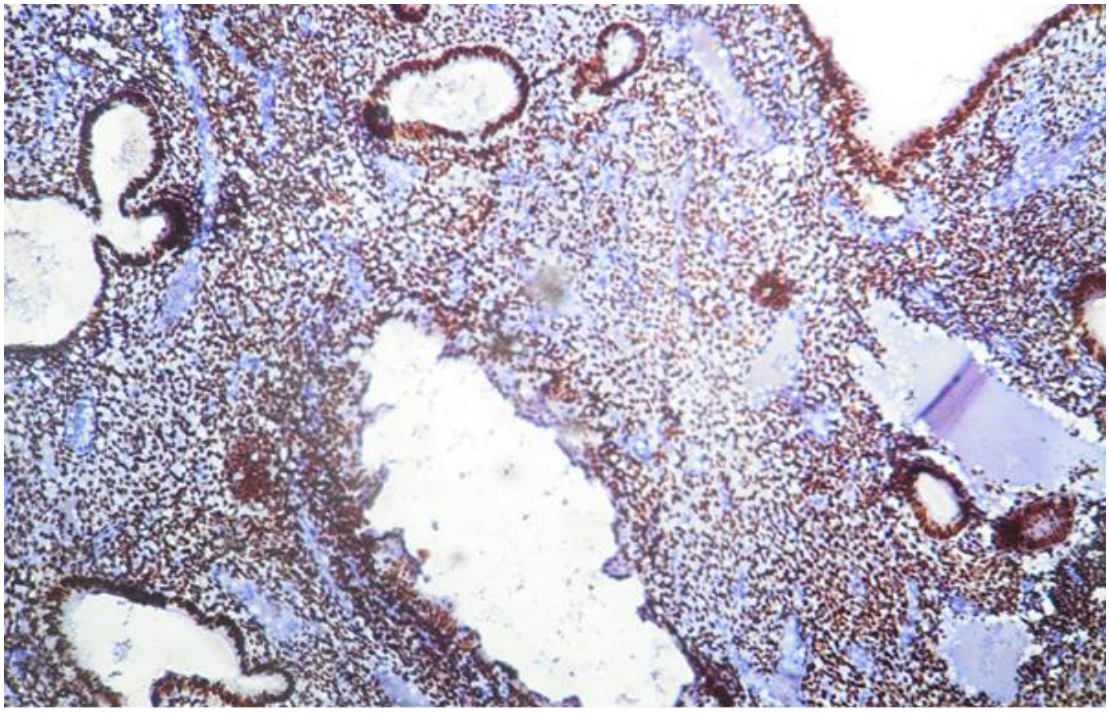


Figure-17. ER expression of simple hyperplasia-moderate nuclear positivity

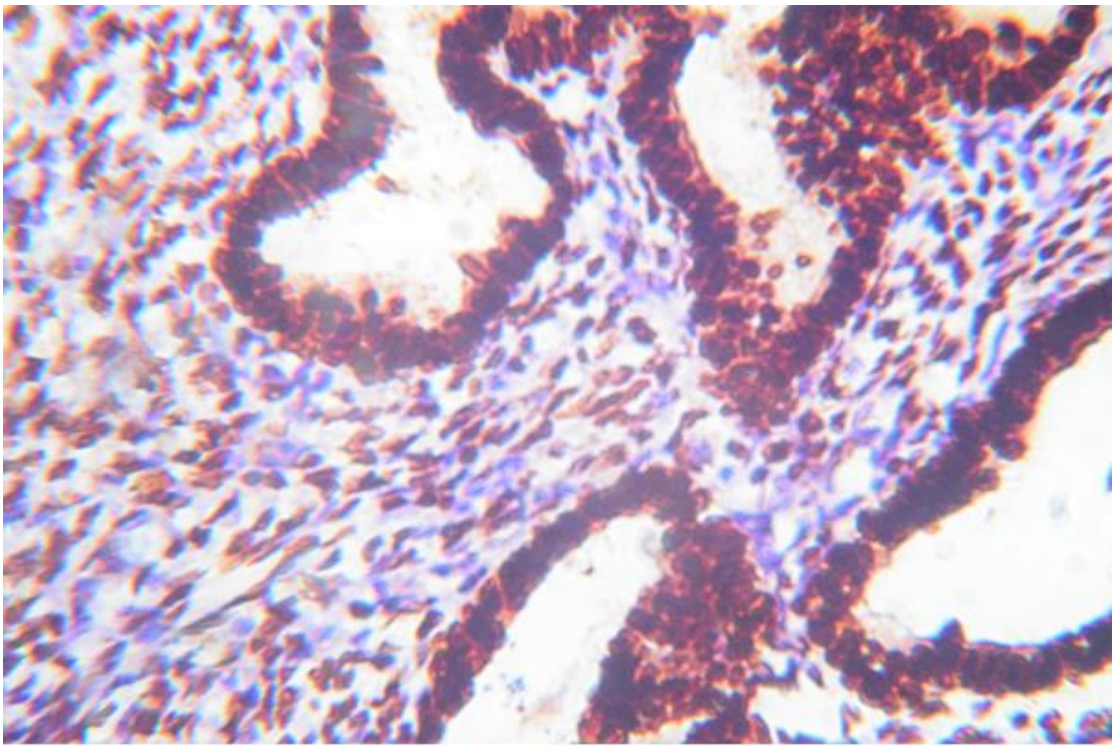


Figure-18. PR expression of simple hyperplasia-moderate nuclear positivity

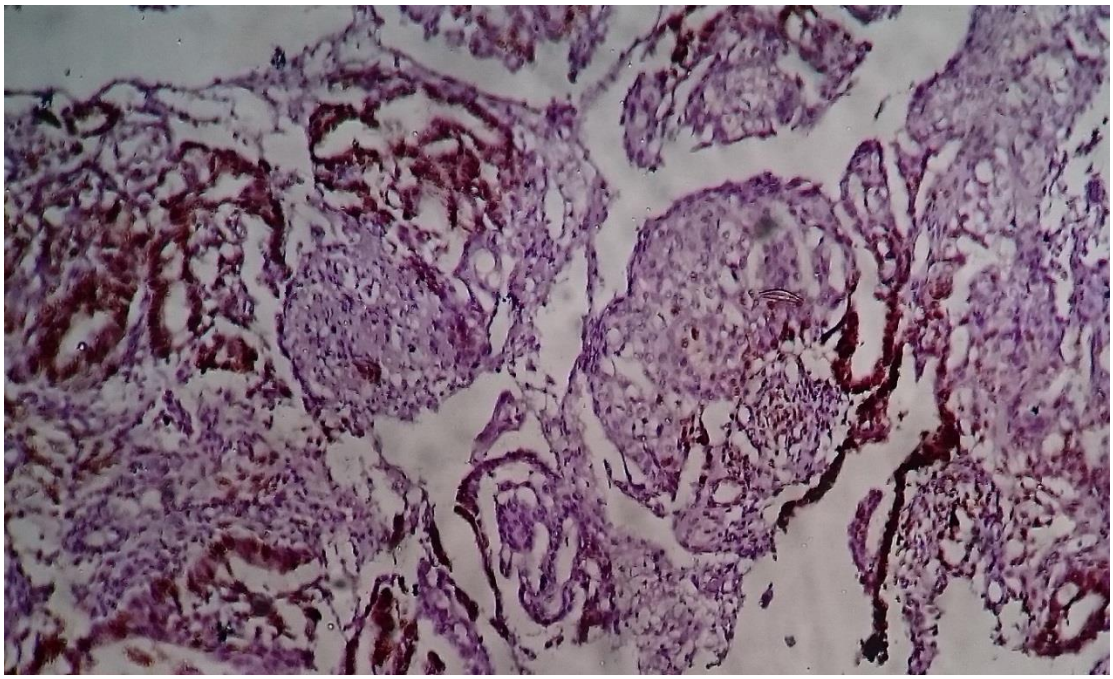


Figure-19. ER expression of endometrial adenocarcinoma showing weak positivity

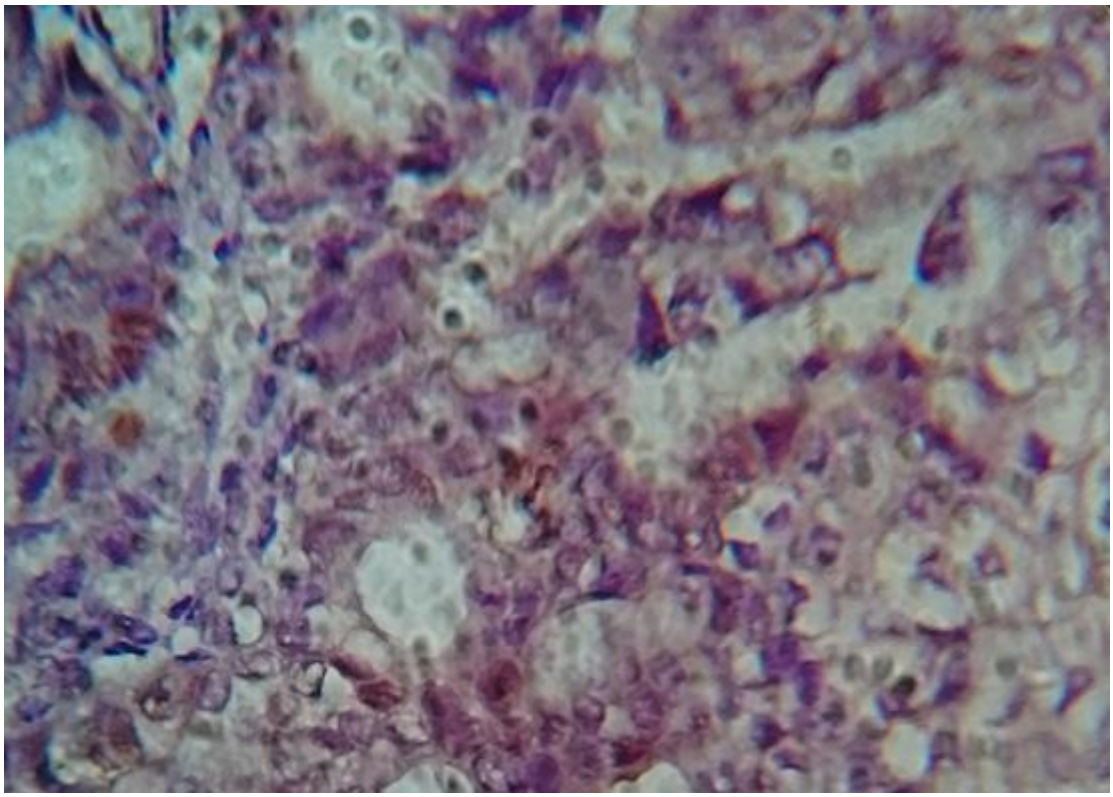


Figure-20. PR expression of endometrial adenocarcinoma showing weak positivity

DISCUSSION

DISCUSSION

Any vaginal bleeding not satisfying the criteria for normal menstruation is called as abnormal uterine bleeding. It is caused by a wide variety of diseases of the reproductive system as well as non-gynaecologic causes. Organic etiologies of AUB include diseases of the reproductive tract, iatrogenic and systemic causes. Dysfunctional uterine bleeding can be diagnosed only after all the organic causes of AUB have been excluded.

The highest incidence of AUB in our study was in the perimenopausal age group (49%) followed by the reproductive age group (42%). This is also the commonest age group affected in most of the studies like Soleymani E et al (37), Shwetha Agrawal et al (38), Jagadale Kunda et al (39).

The most common presenting complaint in this study is menorrhagia (58.7%) followed by metrorrhagia (23.3%). Menorrhagia is also the commonest complaint in many studies like Sadia Khanl et al (40), Sajitha K et al (41), Shwetha Agrawal et al (38) and Jagadale Kunda et al (39). Metrorrhagia is the commonest complaint in studies like Bhatta S et al (42) and Naheed Moghal et al (43). Polymenorrhea is a rare complaint in our study, whereas it is the commonest complaint in Mariam abid et al (44).

AUB can be caused by organic or functional (non-organic) causes. In the most of the studies functional causes are common than organic causes. Likewise, functional causes are slightly more common (53%) than organic causes in this

study. This is comparable to findings in studies like Supriya sandeepa et al (45), Doraiswami saraswathi et al (8), Jagadale Kunda et al (39). In few studies like Nadia Adnan Ghani et al (46), Gerald Dafe Forae et al (47), Mariam abid et al (44) and Smita S Patne et al (48), organic causes are more common than functional causes.

Table-18. Comparative study of incidence of functional and organic causes

S.№	Study	Organic (%)	Non-Organic/ functional (%)
1.	Sadia Khan et al (40)	14	86
2.	Soleymani E et al (37)	18.6	81.4
3.	S. Vaidya et al (49)	19	81
4.	Jagadale Kunda et al (39)	45	55
5.	Supriya sandeepa et al (45)	45.4	53.2
6.	**Present study**	**47**	**53**
7.	Doraiswami saraswathi et al (8)	48.66	51.34
8.	Gerald Dafe Forae et al (47)	57.2	42.8
9.	Mariam abid et al (44)	66	34
10.	Nadia Adnan Ghani et al (46)	61.8	33.5
11.	Smita S Patne et al (48)	75.72	24.28

Table-19. Comparative study of incidence of functional causes of AUB

S.№	Study	Normal cyclical pattern (PP + SP)	DOP	Atrophy
1.	Sadia Khan et al (40)	84	-	1
2.	Soleymani E et al (37)	81.4	15.4	-
3.	Saera Afghan et al (50)	76	-	0.6
4	Shwetha Agrawal et al (38)	71.75	-	-
5.	Pankaj Malukani et al (51)	71	--	7
6.	Zeeba S. Jairajpuri et al (52)	53.91	5.7	1.1
7.	Mahmoud Mohammed Mahmoud et al (53)	51.99	-	4.95
8.	Supriya sandeepa et al (45)	51.1	0.2	1.1
9.	Naheed Moghal et al (43)	49.33	5.02	1.31
10.	Layla S Abdullah et al (54)	46.6	8.7	3.1
11.	Jagadale Kunda et al (39)	44	-	-
12.	Bhatta S et al (42)	42.62	6.56	7.38
13.	Gerald Dafe Forae et al (47)	42.4	-	-
14.	S. Vaidya et al (49)	40.94	13.4	4.71
15.	Bhoomika dadhania et al (55)	36.66	2.66	-
16.	**Present study**	**34.67**	**6.67**	**6**
17.	Sarwat Ara et al (56)	34.16	-	4.34
18.	Mariam abid et al (44)	34	-	6.22
19.	Sajitha K et al (41)	28.9	12.2	5.12
20.	Doraiswami saraswathi et al (8)	28.36	20.53	2.44
21.	Smita S Patne et al (48)	24.28	-	-
22.	Nadia Adnan Ghani et al (46)	23.44	0.68	0.68

PP – proliferative phase; SP – secretory phase

Normal cyclical patterns, including proliferative and secretory patterns are the most common histopathological diagnoses seen in most of the studies. This phenomenon is also seen in this study. Both patterns together constitute 34% of cases in this study. Similar findings are present in Bhoomika dadhania et al

(55) and Sarwat Ara et al (56). Highest incidence of cyclical patterns is observed in Sadia Khan et al (40), Soleymani E et al (37) and Saera Afghan et al (50).

Disordered proliferative endometrium is seen in 6.67% cases in our study. Maximum incidence of this finding (20.53%) is seen in Doraiswami saraswathi et al (8). It is also a common cause of DUB in Soleymani E et al (37), where it accounts for 15.3% cases.

Atrophic endometrium is rarely seen in women of the reproductive age group. It is seen sometimes in perimenopausal women, but it is a common finding in post-menopausal women due to lack of ovarian estrogen. It's incidence in the present study is 6%, which is almost similar to that observed in Mariam abid et al (44) and Sajitha K et al (41). In the present study 7/9 cases of atrophy were seen in women >50 years and 2/9 cases were seen in women aged 41-50 yrs.

Table-20. Comparative study of the incidence of hyperplasia in AUB

S.№	Study	Hyperplasia (% of total causes)	SH	CH	Atypical	N
1.	Smita S Patne et al (48)	41.90	-	-	-	88
2.	**Present study**	**33**	**62.7**	**27.5**	**9.8**	**51**
3.	Sarwat Ara et al (56)	27.94	33.33	53.33	13.33	45
4.	Nadia Adnan Ghani et al (46)	26.89	100	0	0	39
5.	Bhoomika dadhania et al (55)	26.66	45	55	0	40
6.	Sajitha K et al (41)	25	-	-	-	39
7.	Mahmoud Mohammed Mahmoud et al (53)	23.23	57.4	28.7	13.9	122
8.	Jagadale Kunda et al (39)	22	100	0	0	22
9.	Pankaj Malukani et al (51)	22	68.18	27.27	4.55	88
10.	Bhatta S et al (42)	18.03	100	0	0	22
11.	Supriya sandeepa et al (45)	17.4	-	-	-	98
12.	Gerald Dafe Forae et al (47)	17	71.79	12.82	15.38	39
13.	Shwetha Agrawal et al (38)	16.5	100	0	0	66
14.	Sadia Khan et al (40)	12.6	50.79	22.22	26.98	63
15.	Naheed Moghal et al (43)	11.14	82.35	3.92	13.72	51
16.	S. Vaidya et al (49)	10.92	68.18	15.91	15.91	44
17.	Layla S Abdullah et al (54)	9.1	76.92	15.86	7.21	208
18.	Doraiswami saraswathi et al (8)	6.11	-	-	-	25
19.	Zeeba S. Jairajpuri et al (52)	5.79	64.8	13.5	21.6	37
20.	Saera Afghan et al (50)	5.2	4.6	0.6		
21.	Mariam abid et al (44)	5	-	-	54	12
22.	Soleymani E et al (37)	2.5	-	-	-	-

Hyperplasias constitute 33% of cases of AUB in our study. Simple hyperplasia is present in 21.33% cases in this study. A similar incidence of hyperplasia is found in studies like Sarwat Ara et al (56), Nadia Adnan Ghani et

al (46) and Bhoomika dadhania et al (55). Hyperplasia ranks second only to normal cyclical patterns as the cause of AUB in most of the studies. In the present study also hyperplasia is the second common cause of AUB.

The older terminologies like cystoglandular hyperplasia and adenomatous hyperplasia were used in some of the studies. These were replaced my newer terminologies like simple, complex and atypical hyperplasia in recent studies. Comparative analysis of the incidence of hyperplasias in various studies reveal that hyperplasia is a common organic cause of AUB. The highest incidence of hyperplasia is reported in Smita S Patne et al (48) (41.9%), where it was the commonest cause of AUB (common than normal physiological changes). Zeeba S. Jairajpuri et al (52), Saera Afghan et al (50), Mariam abid et al (44) and Soleymani E et al (37) reported a low incidence of hyperplasia. Moderate to heavy vaginal bleeding is seen in women with hyperplasia, whereas women with atrophic endometrium may have only spotting.

The overall risk of progression of hyperplasia to cancer is 5-10%. The risk of progression of simple hyperplasia, complex hyperplasia, simple hyperplasia with atypia and complex hyperplasia with atypia to carcinoma are respectively 1%, 3%, 8% and 29% (57).

Table-21. Comparative study of the incidence of common organic causes of AUB

S.№	Study	Pregnancy complications	Endometritis	Polyp	Malignancy
1.	**Present study**	**-**	**1.33**	**4**	**2**
2.	Sadia Khan et al (40)	-	0.4	0.6	0.4
3.	Soleymani E et al (37)	-	-		0.7
4	Layla S Abdullah et al (54)	-	5.8	9.9	1.8
5.	Mariam abid et al (44)	-	12	14	2
6.	Sajitha K et al (41)	-	0.64	5.12	4.5
7.	Nadia Adnan Ghani et al (46)	20.68	3.44	8.96	1.31
8.	Supriya sandeepa et al (45)	24.1	0.7		1.1
9.	Shwetha Agrawal et al (38)	-	-	-	4.5
10.	Zeeba S. Jairajpuri et al (52)	15.36	6.1	1.72	0.4
11.	Jagadale Kunda et al (39)	18	-	1	4
12.	Bhoomika dadhania et al (55)	-	2	-	2.66
13.	Sarwat Ara et al (56)	16.15	6.21	4.34	1.86
14.	Gerald Dafe Forae et al (47)	27.7	1.3	3.1	3.4
15.	Doraiswami saraswathi et al (8)	22.74	4.15	11.24	4.4
16.	Bhatta S et al (42)	-	6.56	2.46	5.74
17.	Naheed Moghal et al (43)	-	3.28	6.33	0.44
18.	Saera Afghan et al (50)				0.6
19.	Smita S Patne et al (48)	13.8	7.14	5.71	2.38
20.	Mahmoud Mohammed Mahmoud et al (53)	-	3.8	4	2.66
21.	S. Vaidya et al (49)	-	3.23	1.24	2.48
22.	Pankaj Malukani et al (51)	-	-	-	-

Complications of pregnancy are observed as a common cause of abnormal uterine bleeding in some studies like Nadia Adnan Ghani et al (46), Supriya sandeepa et al (45), Zeeba S. Jairajpuri et al (52), Sarwat Ara et al (56), Gerald Dafe Forae et al (47) and Doraiswami saraswathi et al (8). In fact, pregnancy complications was the commonest cause of AUB in Gerald Dafe Forae et al (47). Hence, this cause should be kept in mind when evaluating AUB in women of the reproductive age group. These patients should be investigated with urine gavindex test for pregnancy (58).

The incidence of endometritis in the present study is 1.33%. A high incidence of endometritis is noted in Zeeba S. Jairajpuri et al (52), Sarwat Ara et al (56), Bhatta S et al (42) and Smita S Patne et al (48). In the present study one case of tuberculous endometritis was noted. Doraiswami saraswathi et al (8) and Bhatta S et al (42) each reported one case of tuberculous endometritis. Endometritis was the commonest organic cause of AUB in Zeeba S. Jairajpuri et al (52). In this study, out of 39 cases of endometritis, three were tubercular in origin.

Polyps are an important organic cause of AUB. The present study reported polyps in 4% of cases. Mariam abid et al (44) has the highest incidence of polyps (14% of cases). In this study, there is an increase in frequency of polyps with increasing age. In fact, polyps was the most common pathology in postmenopausal women in this study. Doraiswami saraswathi et al (8) reported the second highest incidence of polyps (11.24%). In this, most of the polyps were

seen in women aged 41-50 yrs. However, there is no greater propensity of polyps undergoing malignant change when compared with the adjacent normal endometrium (59).

Malignancies are less common, but an important cause of abnormal uterine bleeding. In the present study, 3 cases of endometrial carcinoma were seen. Two cases were seen in perimenopausal women and one woman was postmenopausal. Among the malignancies, endometrial carcinoma (especially endometrioid type) was the commonest reported malignancy in most of the studies. Cases of malignant mixed mullerian tumor (MMMT), endometrial stromal sarcoma and adenosarcoma were rarely reported in some studies.

Doraiswami saraswathi et al (8), Shwetha Agrawal et al (38) and Bhatta S et al (42) reported a high incidence of malignancies. Shwetha Agrawal et al (38) reported 18 cases of malignancies of the endometrium of which 14 were endometrial adenocarcinoma, 3 were endometrial stromal sarcoma and one case was MMMT. In Doraiswami saraswathi et al (8), one out the 18 cases of malignancy was malignant mixed mullerian tumor. Patients with MMMT are usually postmenopausal and commonly present with AUB. Nulliparity, increased BMI and chronic anovulation have been implicated as risk factors for endometrial carcinoma.

Table-22. Comparative study of results of present study with other studies

	Present study	Sadia Khan et al (40)	Soleymani E et al (37)	Layla S Abdullah et al (54)	Mariam abid et al (44)
Number of cases	**150**	500	591	2295	241
Type of bleeding	**AUB**	AUB	AUB	AUB	AUB
Common age group	**41-50 (49%)**	45-55 (42%)	41-50 (61.6%)	≥ 52 yrs	Reproductive age group (49.3%)
Common clinical Presentation	**Menorrhagia (58.7%)** **Metrorrhagia (23.3%)**	Menorrhagia (57.8%)			Polymenorrhea (30%) Irregular bleeding (26%)
Common histopathological diagnosis	**Functional (53%) and organic (47%)** **1. Hyperplasia (33%)** **2. PP (20.67%)** **3. SP (14%)** **4. DOP (6.67%)** **5. Atrophy (6%)** **6. Polyps (4%)**	1. PP (46.4%) 2. SP (37.6%) 3. Hyperplasia (12.6%)	1. Normal pathology (PP & SP) (81.4%) 2. DOP (15.4%) 3. Hyperplasia (2.5%)	1. SP (24.9%) 2. PP (21.7%) 3. Polyp (9.9%) 4. Hyperplasia (9.1%) 5. DOP (8.7%)	Organic (66%) and non-organic (34%) 1.Normal menstrual pattern (PP & SP) (34%) 2.Hormonal imbalance pattern (27%) 3.Polyp (14%) 4.Endometritis (12%) 5.Hyperplasia (5%)
Hyperplasia	**1. SH – 32 (62.7%)** **2. CH – 14 (27.5%)** **3. Atypical hyperplasia – 5 (9.8%)**	1. Cystic hyperplasia without atypia (6.4%) 2. Cystic hyperplasia with atypia (2.4%) 3. Adenomatous hyperplasia without atypia (2.8%) 4. Adenomatous hyperplasia with atypia (1.0%)		1. Simple cystic hyperplasia (7%) 2. Complex hyperplasia without atypia (1.4%) 3. Complex hyperplasia with atypia (0.7%)	1. Hyperplasia with atypia (54%) 2. Hyperplasia without atypia (46%)
Frequency of malignancy	**Adenocarcinoma – 2% (n=3); Squamous cell carcinoma infiltrating endometrium (n=1)**	0.4% (n=2)	0.7%	1.8% (n=41); 28/ 41 in ≥ 52 yrs.	2% (n=5)

PP – Proliferative endometrium; SP - secretory endometrium; SH- simple hyperplasia; CH – complex hyperplasia; DOP – disordered proliferative endometrium

	Sajitha K et al (41)	Nadia Adnan Ghani et al (46)	Supriya sandeepa et al (45)	Shwetha Agrawal et al (38)	Zeeba S. Jairajpuri et al (52)
Number of cases	156 (D&C/ Hysterectomy)	152	564	400	638
Type of bleeding	AUB	AUB	AUB	AUB	AUB
Common age group	46-55 (42.95%)	40-55	18-40	41-50	41-50 (35.89)
Common clinical Presentation	Menorrhagia (47%)			Menorrhagia (49%) Menometrorrhagia (22%)	Menorrhagia (41%) Metrorrhagia (18%)
Common histopathological diagnosis	1. Hyperplasia (25%) 2. SP (16.7%) 3. PP (12.2%) 4. DOP (12.2%)	Organic (61.8%) & Non-organic (33.5%) 1. Hyperplasia (26.89%) 2. Pregnancy related bleeding (20.68%) 3. PP (15.86%) 4. SP (7.58%)	Organic (45.4%) & Non-organic (53.2%) 1. PP (27.7%) 2. Pregnancy related lesions (24.1%) 3. SP (23.4%) 4. Hyperplasia (17.4%)	Non-organic (71.75%) & Organic (28.25%) 1.PP (55%) 2.SP (16.75%) 3.Hyperplasia (16.5%) 4.Malignancy (4.5%)	Functional – majority 1. SP (28.99%) 2. PP (24.92%) 3. Pregnancy complications (15.36%) 4. Endometritis (6.1%) 5. Hyperplasia (5.79%) 6. DOP (5.7%)
Hyperplasia	1. SH (12.8%) 2. SH with atypia (3.85%) 3. CH (1.28%) 4. CH with atypia (7.05%)	All hyperplasias are SH without atypia			1. SH (64.8%) 2. CH (13.5%) 3. Atypical (21.6%)
Frequency of malignancy	4.5% (n=7)	N= 2 (1.31%)	1.1% (n=6)	Malignancies n=18 • Endometrial Ca – 14 • Endometrial stromal sarcoma – 3 • Malignant mixed mullerian tumor – 1	0.4% (n=3); all endometrioid with PMB

PP – Proliferative endometrium; SP - secretory endometrium; SH- simple hyperplasia; CH – complex hyperplasia; DOP – disordered proliferative endometrium

	Jagadale Kunda et al (39)	Bhoomika dadhania et al (55)	Sarwat Ara et al (56)	Gerald Dafe Forae et al (47)	Doraiswami saraswathi et al (8)
Number of cases	100	150	161	231	409 [£]
Type of bleeding	AUB	DUB*	AUB	AUB	AUB
Common age group	41-50 (31%)	41-50(40.66%)	36-50 (59.02%)	30-39 (31.2%)	41-50 (33.5%)
Common clinical Presentation	Menorrhagia (88%)		Menorrhagia (49.06%) Metrorrhagia (39.13%)		
Common histopathological diagnosis	1. PP (29%) 2. Hyperplasia (22%) 3. Pregnancy related complications (18%) 4. SP (15%) 5. Polyp (1%)	1.Hyperplasia (26.66%) 2.PP (21.33%) 3.SP (15.33%)	1. Hyperplasia (27.94%) 2. PP (21.74%) 3. Pregnancy complications (16.15%) 4. SP (12.42%)	1.Products of conception (27.7%) 2.PP (22.5%) 3.SP (19.9%) 4.Hyperplasia (17%)	Isolated endometrial pathology on 409 cases 1. Normal cyclical pattern (PP, SP & shedding) (28.36%) 2. Complications of pregnancy (22.74%) 3. DOP (20.53%) 4. Polyp (11.24%) 5. Hyperplasia (6.11%)
Hyperplasia	All hyperplasias are SH without atypia	1.Adenomatous hyperplasia (13.33%) 2.Simple cystic hyperplasia (12%) 3.CH (1.33%)	1. Adenomatous hyperplasia (14.91%) 2. Cystic glandular hyperplasia (9.31%) 3. Atypical hyperplasia (3.72%)	1.SH (12.2%) 2.CH (2.2%) 3.Atypical (2.6%)	
Frequency of malignancy	4% (n=4)	2.66% (n=4); all cases in patients > 50 yrs.	1.86% (n=3)	3.4% (n=8) Endometrial Ca (n=4) MMMT[≠] (n=3) Choriocarcinoma (n=1)	4.4% (n=18)

***** Though the term DUB (which refers to the functional/non-organic cause of AUB) was used in the study, the organic causes like hyperplasia and adenocarcinoma are also included

[≠] Malignant mixed mullerian tumor

[£] Out of 620 cases (408 samples+ 212 hysterectomy), 211 cases with leiomyoma, adenomyosis and cervical pathology with or without endometrial lesions were excluded from the study. The remaining 409 patients with isolated endometrial pathology were included in the study

	Bhatta S et al (42)	Naheed Moghal et al (43)	Saera Afghan et al (50)	Smita S Patne et al (48)	Mahmoud Mohammed Mahmoud et al (53)
Number of cases	122	458	150	210	525
Type of bleeding	AUB	AUB	AUB	AUB	AUB
Common age group			31-40 (47.2%)	31-40 (33.8%)	41-50
Common clinical Presentation	Metrorrhagia (38.52%) Menorrhagia (30.32%)	Metrorrhagia (48.04%) Menorrhagia (40.83%)	Menorrhagia (34%) Polymenorrhagia (27%)	Menorrhagia (42.85%) Metrorrhagia (28.09%)	Menorrhagia (42.7%) Menometrorrhagia (18.9%)
Common histopathological diagnosis	1. PP (26.23%) 2. Hyperplasia (18.03%) 3. SP (16.39%) 4. Atrophic (7.38%)	1.SP (25.33%) 2.PP (24%) 3.Hyperplasia (11.14%) 4.DOP (5.02%)	1. Normal physiological changes (PP & SP) (76%) 2. Hyperplasia (5.2%) 3. Pill pattern (7.3%)	1. Hyperplasia (41.90%) 2. PP (24.28%) 3. Pregnancy complications [β] (13.8%) 4. Endometritis (7.14%) 5. Polyp (5.71%)	Organic (38.7%) and non-organic (61.3%) 1. PP (30.28%) 2. Hyperplasia (23.23%) 3. SP (21.71%) 4. Atrophy (4.95%) 5. Polyp (4%) 6. Endometritis (3.8%)
Hyperplasia	All hyperplasia SH without atypia (18.03%)	1. SH (n=42) 2. CH (n=2) 3. Atypical (n=7)	1. Cystic hyperplasia (4.6%) 2. Adenomatous hyperplasia (0.6%)		1. SH (57.4%) 2. CH without atypia (28.7%) 3. CH with atypia (13.9%)
Frequency of malignancy	5.74% (n=7)	Endometrial Ca – 0.44% (n=2) Adenosarcoma – 0.21% (n=1)	0.6% (n=1)	2.38% (n=5)	2.66% (n=14); all cases > 50 yrs

[β] Pregnancy related complications include products of conception, and partial and complete hydatiform mole

	S. Vaidya et al (49)	Pankaj Malukani et al (51)
Number of cases	403	400
Type of bleeding	AUB	DUB [μ]
Common age group	41-50	31-40 (48%)
Common clinical Presentation		Menorrhagia (76.5%) Metrorrhagia (13.5%)
Common histopathological diagnosis	Functional (81%) and organic (19%) 1. SP (22.58%) 2. PP (18.36%) 3. DOP (13.4%) 4. Hyperplasia (10.92%)	1.PP (39.75%) 2.SP (31.25%) 3.Hyperplasia (22%) 4.Atrophy (7%)
Hyperplasia	1. SH -30 (68.18%) 2. CH -7 (15.91%) 3. Atypical Hyperplasia -7 (15.91%)	1.SH – 60 (68.18%) 2.CH – 24 (27.27%) 3.Atypical hyperplasia – 4 (4.55%)
Frequency of malignancy	2.48% (n=10)	

[μ] Though the term DUB (which refers to the functional/non-organic cause of AUB) was used in the study, the organic cause like hyperplasia were also included.

Table-23. Comparative study of age-wise distribution of various histopathological diagnosis of present study with other studies

S.№	Diagnosis	Present study				Layla S Abdullah et al (54)				Mariam abid et al (44)			
		18-40 (63)	41-50 (74)	>50 (13)	Total (150)	19-39 (700)	40-51 (735)	>51 (860)	Total (2295)	12-39 (119)	40-50 (77)	>50 (45)	Total (241)
1.	Pr	14 (22.2%)	17 (23%)	0	31 (20.67%)	222 (31.7%)	113 (15.4%)	163 (19%)	498 (21.7%)	61 (51%)	21 (27.3%)	0	82 (34%)
2.	Sec	10 (15.9%)	11 (14.9%)	0	21 (14%)	246 (35%)	122 (16.6%)	203 (23.6%)	571 (24.9%)				
3.	Hyperplasia	26 (41.3%)	22 (29.72%)	3 (23.07%)	51 (34%)	39 (5.54%)	94 (12.84%)	75 (8.8%)	208 (9.1%)	1 (1%)	5 (6.5%)	6 (13.2%)	12 (5%)
4.	DOP	4 (6.3%)	5 (6.8%)	1 (7.7%)	10 (6.67%)	46 (6.6%)	85 (11.6%)	69 (8%)	200 (8.7%)	0	0	0	0
5.	Polyp	3 (4.81%)	3 (4.1%)	0	6 (4%)	39 (5.6%)	75 (10.2%)	113 (13.1%)	227 (9.9%)	10 (8.4%)	8 (10.4%)	16 (35.5%)	34 (14%)
6.	Endometritis	0	2 (2.7%)	0	2 (1.33%)	44 (6.3%)	53 (7.2%)	37 (4.3%)	134 (5.8%)	21 (18%)	7 (9.1%)	0	28 (12%)
7.	Atrophy	0	2 (2.7%)	7 (53.81%)	9 (6%)	0	21 (2.9%)	49 (5.7%)	70 (3.1%)	0	0	15 (33.3%)	15 (6.2%)
8.	Carcinoma	0	2 (2.7%)	1 (7.7%)	3 (2%)	2 (0.3%)	11 (1.5%)	28 (3.3%)	41 (1.8%)	0	1 (1.2%)	4 (9%)	5 (2%)

Estrogen and progesterone are consistently produced by the ovaries. The endometrium is a highly sensitive indicator of the hypothalamic-pituitary-ovarian axis. Both endometrial glandular and stromal cells have estrogen and progesterone receptors. The hormonal control is mediated by these receptors. Estradiol increases both ER and PR, while progesterone decreases both receptors.

The present study compared the immunohistochemical staining of ER and PR between non-malignant endometrium and malignant endometrium. The non-malignant endometrium studied include proliferative pattern and all types of hyperplasia. This study showed that most of non-malignant endometrium showed positivity for estrogen receptors (94.1%) and progesterone receptors (96.9%). Quantitative analysis of the steroid hormone receptors (the number of positively stained cells divided by the total number of cells counted= percentage index) revealed that the mean of the Percentage Index of all the proliferative endometrium was the highest (91.64% for ER and 94.38% for PR) followed by simple hyperplasia, complex hyperplasia and atypical hyperplasia. It was also observed that the mean of the PI values for both ER and PR were the lowest for endometrial adenocarcinoma (27.5% for ER and 27% for PR). The mean values of PI for PR were slightly higher than that for ER.

Mylonas et al (60) compared the expression for ER and PR of normal human endometrium (proliferative and secretory) with that of malignant endometrium. The study revealed that ER and PR expression declined

significantly in the glandular epithelium when going from proliferative (high expression) to the secretory phase (low expression). The expression of the hormone receptors was lowest with adenocarcinoma.

Daniela Ilie et al (61) compared the index to ER and PR positivity in the glandular epithelium of normal endometrium, hyperplastic endometrium and endometrial carcinoma. This study noted that the expression of ER and PR was predominant in the proliferative phase compared with the secretory phase. The ER and PR expression decreased in the hyperplastic and neoplastic endometrium compared with that of the proliferative phase. This study that among the hyperplasias, the mean PI for ER and PR was high in case of complex hyperplasia without atypia (mean PI for ER 72.3%; mean PI value for PR of 78.5%) followed by atypical hyperplasia and simple hyperplasia. This is in contrast with our study which found that simple hyperplasia has high mean PI value (60.2% for ER; 65.33% for PR) followed by complex hyperplasia and atypical hyperplasia in that order. However, this study also found that endometrial carcinoma has the lowest value of mean PI which is similar to that observed in our study.

Sahar Aly Daoud et al (62) compared the expression of ER and PR immunostaining in normal and hyperplastic endometrium with that of malignant endometrium. This is a qualitative study which studied the number of positive cases for ER and PR in each group. It found that among 28 cases of non-malignant endometrium 22 (78.57%) were positive for ER and 19 (67.85%) were

positive for PR. Among 20 cases of endometrial carcinoma, 14 (70%) were positive for ER and 12 were positive for PR (60%).

CONCLUSION

CONCLUSION

AUB is one of the common reasons for visit to the gynaecology outpatient department.

The present study showed that the highest incidence of AUB is in the perimenopausal age group (41-50 years).

Simple hyperplasia is the commonest histological diagnosis followed by the proliferative and secretory pattern.

Immunohistochemistry reveals that ER and PR expression decreases progressively as we go from the proliferative pattern through hyperplasias to adenocarcinoma.

ER and PR expression in endometrial adenocarcinoma is of prognostic significance. PR positive tumors may be amenable to hormone therapy of women who wish to retain their fertility and non-surgical patients.

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DR. A.R. Chakravarthi, M.D., D.G.O.
Dean

Date : .....

15.09.2015

The Ethical Committee met on 16.12.2013 and Dr. S. Manjani, Register No-201313552, Post Graduate Student in the Department of Pathology has presented the following topic and the committee approved the same.

"HISTOPATHOLOGICAL STUDY OF ENDOMETRIAL CURETTINGS ON WOMEN WITH ABNORMAL UTERINE BLEEDING AND IMMUNOHISTOCHEMICAL STUDY OF ESTROGEN AND PROGESTERONE RECEPTOR EXPRESSION IN PERIMENOPAUSAL GROUP"

DEAN

DEAN
KARPAGA VINAYAGA INSTITUTE
OF MEDICAL SCIENCES
G.S.T. ROAD, PALAYANOOR POST
MADURANTHAGAM TALUK

ANNEXURES

ANNEXURES

ANNEXURE A

DATA COLLECTION FORM

NAME : **DATE:**

AGE :

I.P.№ :

WEIGHT :

PARITY :

CHIEF COMPLAINTS :

PAST MEDICAL HISTORY :

MENSTRUAL HISTORY :

GROSS FINDINGS :

HISTOPATHOLOGICAL FINDINGS:

ANNEXURE B

STAINING TECHNIQUE

Hematoxylin and Eosin (H& E)

Procedure

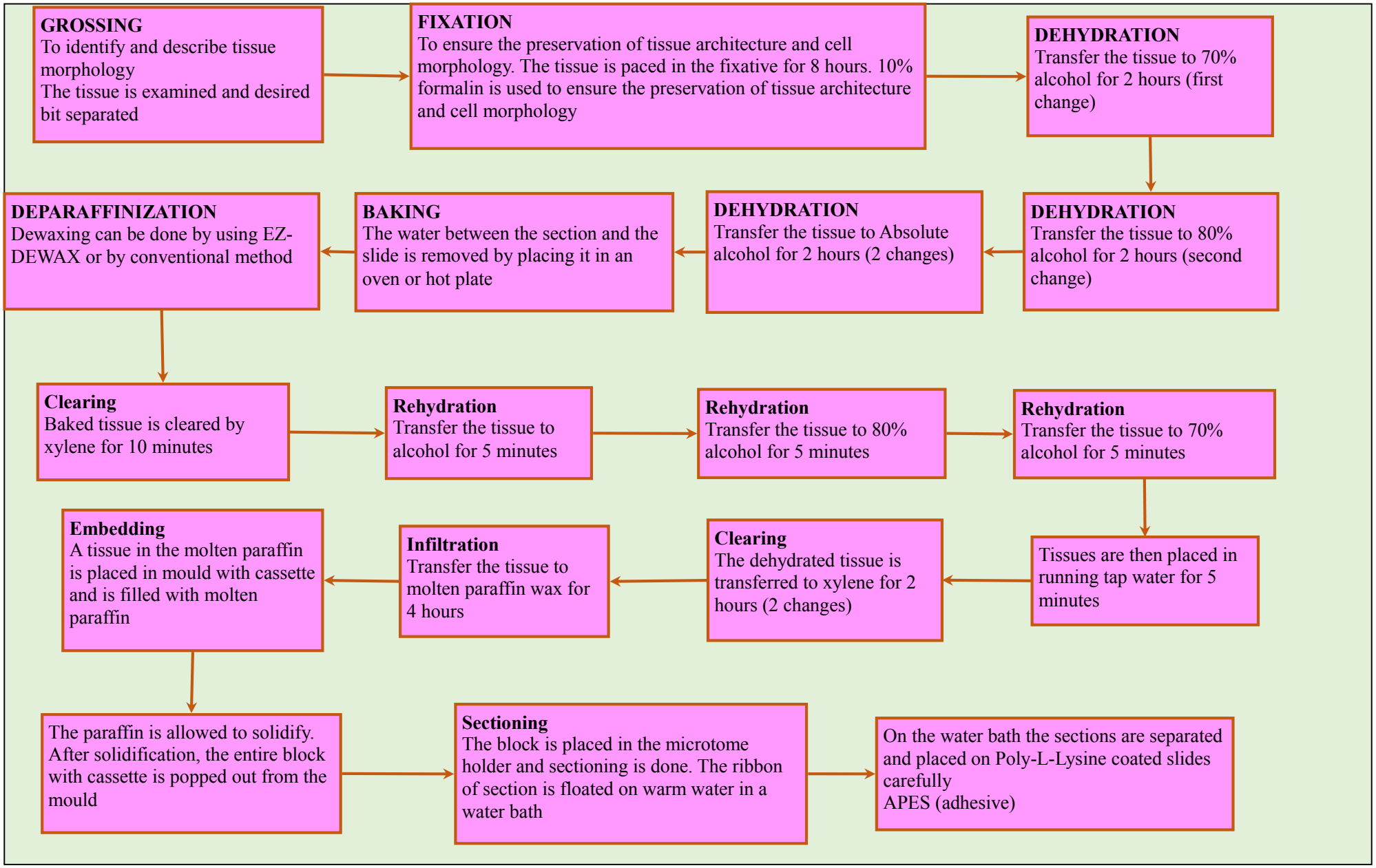
1. Bring sections to water
2. Stain with Harris Hematoxylin for 2-3 minutes
3. Wash with running tap water
4. Differentiate in 1% acid alcohol
5. Wash and blue with running tap water
6. Counter stain with aqueous eosin for 2 minutes
7. Dehydrate with absolute alcohol (2-3 changes)
8. Clear with 2-3 changes of xylene
9. Mount using Dibutyl phthalate polystyrene xylene (Dpx)

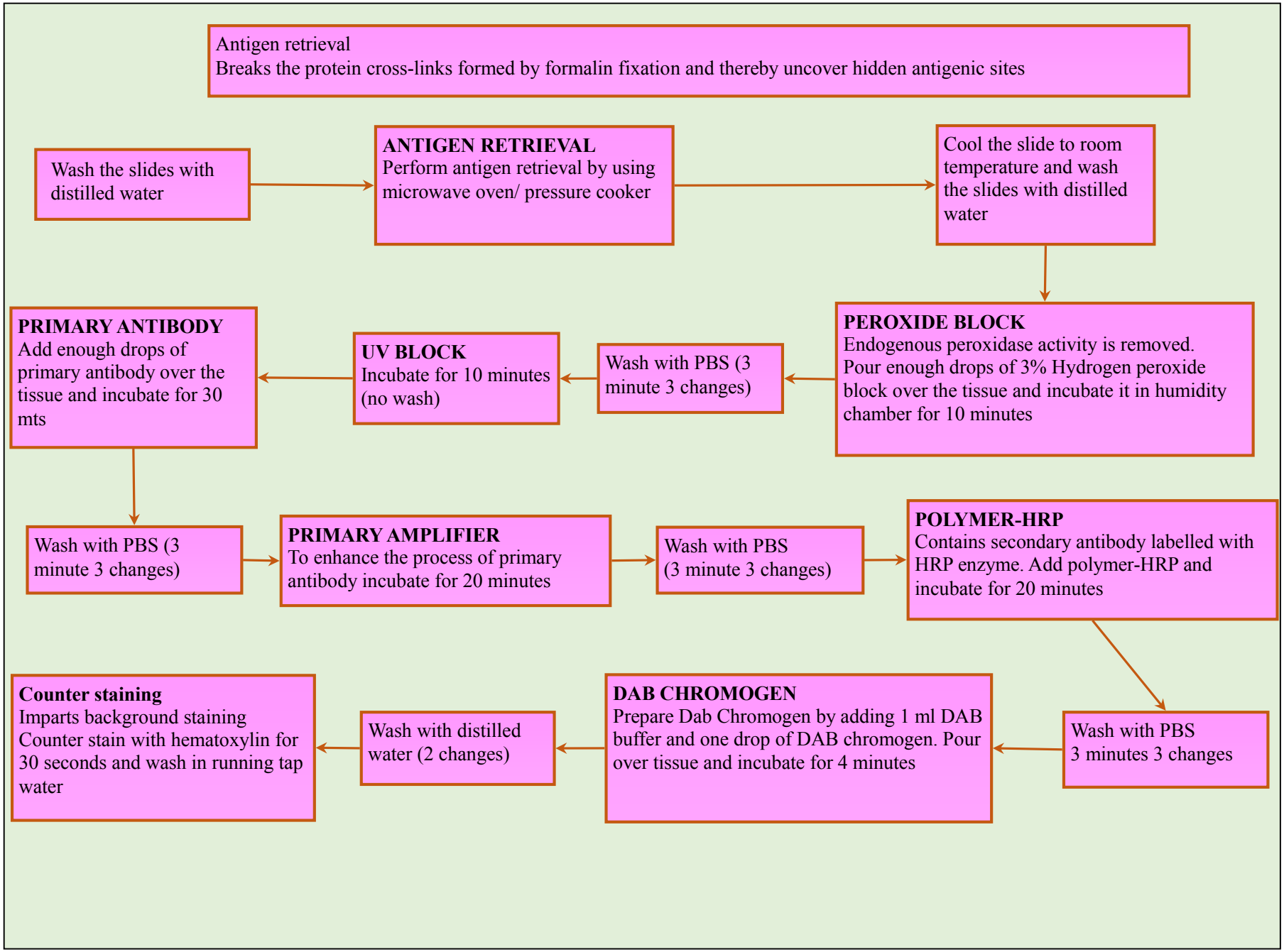
Results

Nucleic acid – blue

Cytoplasm – pink

ANNEXURE C: FLOW CHART FOR IMMUNOHISTOCHEMISTRY




Antigen retrieval
Breaks the protein cross-links formed by formalin fixation and thereby uncover hidden antigenic sites
Wash the slides with distilled water
ANTIGEN RETRIEVAL
Perform antigen retrieval by using microwave oven/ pressure cooker
Cool the slide to room temperature and wash the slides with distilled water
PEROXIDE BLOCK
Endogenous peroxidase activity is removed. Pour enough drops of 3% Hydrogen peroxide block over the tissue and incubate it in humidity chamber for 10 minutes
Wash with PBS (3 minute 3 changes)
UV BLOCK
Incubate for 10 minutes (no wash)
PRIMARY ANTIBODY
Add enough drops of primary antibody over the tissue and incubate for 30 mts
Wash with PBS (3 minute 3 changes)
PRIMARY AMPLIFIER
To enhance the process of primary antibody incubate for 20 minutes
Wash with PBS (3 minute 3 changes)
POLYMER-HRP
Contains secondary antibody labelled with HRP enzyme. Add polymer-HRP and incubate for 20 minutes
Wash with PBS 3 minutes 3 changes
DAB CHROMOGEN
Prepare Dab Chromogen by adding 1 ml DAB buffer and one drop of DAB chromogen. Pour over tissue and incubate for 4 minutes
Wash with distilled water (2 changes)
Counter staining
Imparts background staining
Counter stain with hematoxylin for 30 seconds and wash in running tap water

ANNEXURE - D

LIST OF ABBREVIATIONS

SH – Simple Hyperplasia

CH – Complex Hyperplasia

PP – Proliferative Pattern

SP – Secretory Pattern

DOP – Disordered Proliferative Endometrium

AUB – Abnormal Uterine Bleeding

DUB – Dysfunctional Uterine Bleeding

FSH – Follicle Stimulating Hormone

LH – Luteinizing Hormone

HRT – Hormone Replacement Therapy

HRP – Horse Radish Peroxidase

VEGF – Vascular Endothelial Growth Factor

ANNEXURE - E

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

Figure-14	Secretory Exhaustion
Figure-15	ER of proliferative endometrium-40x magnification strong and intense nuclear positivity
Figure-16	PR of proliferative endometrium-40x magnification strong and intense nuclear positivity
Figure-17	ER expression of simple hyperplasia-moderate nuclear positivity
Figure-18	PR expression of simple hyperplasia-moderate nuclear positivity
Figure-19	ER expression of endometrial adenocarcinoma showing weak positivity
Figure-20	PR expression of endometrial adenocarcinoma showing weak positivity

ANNEXURE - F

KEY TO MASTER CHART

AUB – Abnormal Uterine Bleeding

MR – Menorrhagia

MTR – Metrorrhagia

MMTR – Menometrorrhagia

PMR – Polymenorrhea

PMB – Postmenopausal Bleeding

ANNEXURE – G: MASTER CHART

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
1	Mrs Kumari	46	604/13	2907130010	P3	+					AUB	ET-10mm	Secretory pattern
2	Mrs.Samans Mary	42	614/13	270713002	P3		+				AUB	ET-8mm	Secretory pattern
3	Mrs.Padmavathy	45	641/13	0808130028	P2	+					AUB	ET-7mm	Proliferative pattern
4	Mrs Mohana Tirunavukarasu	48	659/13	0708130013	P3		+				AUB	ET-11mm	Complex hyperplasia
5	Mrs.Banumathy	65	671/13	0208130036	P4					+	AUB	ET-4mm	Atrophic endometrium
6	Mrs.Lakshmi	45	726/13	0309130076	P3				+		AUB	ET-10mm	Simple hyperplasia
7	Mrs.Sujatha	37	780/13	1010130008	P2		+				AUB	ET-10mm	Simple hyperplasia
8	Mrs.Shanthi	50	782/13	0110130007	P3			+			AUB	ET-7mm	Chronic endometritis
9	Mrs.Pushnavathi	43	796/13	1710130007	P2	+					AUB	ET-6mm	Atypical hyperplasia
10	Mrs.Nagammal	60	809/13	0110130006	P4					+	AUB	ET-6mm	Squamous cell carcinoma infiltrating endometrium
11	Mrs.Vasanthi	38	821/13	1710130022	P2	+					AUB	ET-15mm	Complex hyperplasia
12	Mrs .Thangam	58	832/13	2810130015	P3					+	AUB	ET-6mm	Simple hyperplasia
13	Mrs.Gomathi	42	865/13	1911130003	P3	+					AUB	ET-5mm	Menstrual phase
14	Mrs.Manogari	30	916/13	1912130007	P2	+					AUB	ET-6mm	Complex hyperplasia
15	Mrs.Chinnakulandhai	50	919/13	1612130029	P3		+				AUB	ET-8mm	Chronic endometritis
16	Mrs.Shantha	48	925/13	2612130015	P3		+				AUB	ET-4mm	Secretory hyperplasia
17	Mrs.Sumathi	36	926/13	2612130074	P2			+			AUB	ET-11mm	Atypical hyperplasia

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
18	Mrs.Deepa	40	927/13	2612130016	P3	+					AUB	ET-11mm	Simple hyperplasia
19	Mrs.Janagavali	40	039/14	1701140009	P3		+				AUB	ET-9mm	Secretory hyperplasia
20	Mrs.Umamaheswari	42	046/14	2401140014	P2	+					AUB	ET-5mm	Secretory pattern
21	Mrs.Valarmathy	42	051/14	0201140040	P2	+					AUB	ET-6mm	Secretory pattern
22	Mrs.Chellammal	49	102/14	1002140062	P3		+				AUB	ET-9mm	Proliferative pattern
23	Mrs.Amishiya	45	107/14	1202140042	P3	+					AUB	ET-5mm	Simple hyperplasia
24	Mrs.Saraswathy	48	109/14	1302140030	P3	+					AUB	ET-12mm	Irregular shedding
25	Mrs.Saraswathy	40	180/14	0803140004	P1	+					AUB	ET-5mm	Endometrial polyp
26	Mrs.Sumathy	36	190/14	0503140021	P2		+				AUB	ET-6mm	Simple hyperplasia
27	Mrs.Bhuvaneswari	40	206/14	1903140012	P3		+				AUB	ET-11mm	Simple hyperplasia
28	Mrs.Selvi	50	213/14	2103140002	P2	+					AUB	ET-10mm	Simple hyperplasia
29	Mrs.Jayanthi	32	226/14	1803140006	P2	+					AUB	ET-6mm	Secretory pattern
30	Mrs.Rajeswari	38	230/14	2603140005	P2	+					AUB	ET-13mm	Secretory hyperplasia
31	Mrs.Kamatchi	51	273/14	0704140004	P2					+	AUB	ET-10mm	Atrophic endometrium
32	Mrs.Papammal	40	276/14	2703140045	P2		+				AUB	ET-9mm	Simple hyperplasia
33	Mrs.Kasthuri	43	285/14	0404140051	P3		+				AUB	ET-14mm	Simple hyperplasia
34	Mrs.Thayammal	38	295/14	1204140003	P2		+				AUB	ET-15mm	Atypical hyperplasia
35	Mrs.Neela	40	296/14	0804140060	P3	+					AUB	ET-6mm	Secretory pattern
36	Mrs.Vasntha	39	309/14	1504140013	P2	+					AUB	ET-12mm	Complex hyperplasia

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
37	Mrs.Kanniga	42	314/14	1604140007	P2	+					AUB	ET-5mm	Complex hyperplasia
38	Mrs.Lakshmi	49	323/14	1804140003	P3		+				AUB	ET-10mm	Endometrial adenocarcinoma
39	Mrs .Chandra	48	324/14	1904140001	P2	+					AUB	ET-6mm	Atrophic endometrium
40	Mrs.Suguna	42	359/14	2704140003	P3	+					AUB	ET-6mm	Menstrual phase
41	Mrs.Vasantha	38	367/14	2804140029	P2	+					AUB	ET-5mm	Secretory pattern
42	Mrs.Sathya	30	375/14	0505140047	P2	+					AUB	ET-7mm	Disordered proliferative endometrium
43	Mrs.Sagunthala	45	388/14	0505140053	P2		+				AUB	ET-10mm	Complex hyperplasia
44	Mrs.Kamatchi	37	389/14	0705140033	P2	+					AUB	ET-11mm	Simple hyperplasia
45	Mrs.Radha	50	392/14	0505140049	P3	+					AUB	ET-6mm	Complex hyperplasia
46	Mrs.Sellamallal	50	416/14	1205140053	P2	+					AUB	ET-5mm	Simple hyperplasia
47	Mrs.Kanchana	44	419/14	1305140002	P2	+					AUB	ET-8mm	Complex hyperplasia
48	Mrs.Ajantha	44	420/14	1405140046	P3		+				AUB	ET-polyp	Endometrial polyp
49	Mrs.Eganthal	45	429/14	1505140052	P3	+					AUB	ET-10mm	Proliferative pattern
50	Mrs.Dhanalakshmi	28	445/14	1505140046	P3	+					AUB	ET-polyp	Complex hyperplasia
51	Mrs.Devi	28	452/14	2105140016	P2	+					AUB	ET-6mm	Simple hyperplasia
52	Mrs.Panchalai	42	475/14	1505140054	P4	+					AUB	ET-5mm	Secretory pattern
53	Mrs.Kasthuri	33	485/14	2905140009	P2	+					AUB	ET-polyp	Endometrial polyp
54	Mrs.Pooniyammal	37	500/14	0306140008	P2	+					AUB	ET-6mm	Proliferative pattern
55	Mrs.Sumathy	36	506/14	0506140001	P2	+					AUB	ET-10mm	Proliferative pattern

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
56	Mrs.Barathi	23	516/14	0906140016	P2	+					AUB	ET-6mm	Menstrual phase
57	Mrs.Saraswathy	48	545/14	1606140008	P4		+				AUB	ET-5mm	Simple hyperplasia
58	Mrs.Vedhavalli	49	550/14	1906140049	P2	+					AUB	ET-6mm	Complex hyperplasia
59	Mrs.Adhilakshmi	44	559/14	2106140007	P3	+					AUB	ET-11mm	Granulomatous TB
60	Mrs.Poonammal	45	566/14	2306140003	P2	+					AUB	ET-11mm	Secretory hyperplasia
61	Mrs.Shanthi Mahadevan	44	576/14	1006140046	P2		+				AUB	ET-pyometra	Secretory pattern
62	Mrs.Manjula	40	581/14	2706140004	P3		+				AUB	ET-4mm	Secretory pattern
63	Mrs.Myli	29	622/14	0907140018	P2	+					AUB	ET-15mm	Proliferative pattern
64	Mrs.Parvathy	40	643/14	1407140020	P2	+					AUB	ET-6mm	Menstrual phase
65	Mrs.Alamelu	49	683/14	2607140044	P3	+					AUB	ET-7mm	Proliferative pattern
66	Mrs.Dhavamani	32	688/14	3007140021	P2	+					AUB	ET-7mm	Simple hyperplasia
67	Mrs.Chellamal	50	708/14	2107140011	P3		+				AUB	ET-10mm	Simple hyperplasia
68	Mrs.Jaya	28	720/14	3107140047	P2	+					AUB	ET-5mm	Proliferative pattern
69	Mrs.Kanaga	42	735/14	0808140007	P2		+				AUB	ET-8mm	Mixed pattern
70	Mrs.Shanthi	47	736/14	01081400521	P2			+			AUB	ET-10mm	Simple hyperplasia
71	Mrs.Bavani	38	738/14	0508140023	P2	+					AUB	ET-11mm	Simple hyperplasia
72	Mrs.Geetha	54	743/14	0408140025	P3					+	AUB	ET-11mm	Simple hyperplasia
73	Mrs.Renuga	46	753/14	0408140061	P3	+					AUB	ET-10mm	Proliferative pattern

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
74	Mrs.Susila	42	768/14	1608140009	P3		+				AUB	ET-8mm	Disordered proliferative endometrium
75	Mrs.Yasodha	40	773/14	1808140070	P2	+					AUB	ET-10mm	Disordered proliferative endometrium
76	Mrs.Lalitha	48	791/14	2308140011	P2	+					AUB	ET-11mm	Atypical hyperplasia
77	Mrs.Dilliyammal	45	807/14	0308140014	P2	+					AUB	ET-8mm	Secretory pattern
78	Mrs.Lakshmi Suresh	40	813/14	1508140011	P0	+					AUB	ET-6mm	Proliferative pattern
79	Mrs.Lakshmi Madhavan	38	821/14	0109140032	P1	+					AUB	ET-10mm	Proliferative pattern
80	Mrs.Ellammal	45	822/14	0209140015	P2			+			AUB	ET-11mm	Proliferative pattern
81	Mrs.Sarasu	50	845/14	0809140021	P3		+				AUB	ET-9mm	Disordered proliferative endometrium
82	Mrs.Kuppu	46	849/14	0609140056	P2	+					AUB	ET-8mm	Complex hyperplasia
83	Mrs.Meena	50	860/14	0509140049	P2			+			AUB	ET-9mm	Disordered proliferative endometrium
84	Mrs.Selvi	52	880/14	1809140011	P3					+	AUB	ET-6mm	Disordered proliferative endometrium
85	Mrs.Munniyammal	40	882/14	2009140034	P2			+			AUB	ET-5mm	Secretory pattern
86	Mrs.Poornima	30	892/14	2309140025	P1	+					AUB	ET-11mm	Arias stella effect
87	Mrs.Lakshmi	44	893/14	2309140004	P2	+					AUB	ET-5mm	Proliferative pattern
88	Mrs.Amudha	50	902/14	2509140029	P2	+					AUB	ET-polyp	Endometrial polyp
89	Mrs.	52	924/14	2409140015	P4					+	AUB	ET-12mm	Endometrial adenocarcinoma
90	Mrs.Selvi	35	935/14	0710140027	P2	+					AUB	ET-polyp	Endometrial polyp

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
91	Mrs.Vijaya	44	947/14	0910140019	P3		+				AuB	ET-10mm	Proliferative pattern
92	Mrs.Rukumani	30	948/14	091040017	P2	+					AUB	ET-6mm	Proliferative pattern
93	Mrs.Krishnamani	47	960/14	1110140034	P3	+					AUB	ET-10mm	Secretory pattern
94	Mrs.Valli	38	969/14	0710140029	P2			+			AUB	ET-11mm	Simple hyperplasia
95	Mrs.Latha	38	970/14	1410140025	P2	+					AUB	ET-7mm	Disordered proliferative endometrium
96	Mrs.Kanniyammal	50	979/14	1610140010	P3		+				AUB	ET-4mm	Proliferative pattern
97	Mrs.Sankari	41	996/14	2510140015	P2	+					AUB	ET-5mm	Secretory pattern
98	Mrs.Karpagavalli	36	997/14	2310140025	P2	+					AUB	ET-8mm	Proliferative pattern
99	Mrs.Dhulasi	60	1000/14	2710140024	P4					+	AUB	ET-10mm	Atrophic endometrium
100	Mrs.Laksmi	39	1010/14	2910140001	P2	+					AUB	ET-12mm	Complex hyperplasia
101	Mrs.Alamelu	45	1018/14	0111140033	P3	+					AUB	ET-10mm	Proliferative pattern
102	Mrs.Malliga	50	1024/14	3110140077	P3		+				AUB	ET-15mm	Simple hyperplasia
103	Mrs.Pushpavathy	41	1036/14	3110140003	P2				+		AUB	ET-20mm	Simple hyperplasia
104	Mrs.Rukmani	33	1038/14	0811140035	P2	+					AUB	ET-6mm	Proliferative pattern
105	Mrs.Sarasu	40	1045/14	1211140040	P2	+					AUB	ET-12mm	Proliferative pattern
106	Mrs.Sathiya Priya	32	1060/14	1811140012	P2	+					AUB	ET-15mm	Simple hyperplasia
107	Mrs.Thilagam	40	1073/14	2511140009	P2	+					AUB	ET-14mm	Simple hyperplasia
108	Mrs.Paanjalai	52	1078/14	2411140036	P3					+	AUB	ET-4mm	Atrophic endometrium
109	Mrs.Valliyammal	39	1080/14	2611140005	P2		+				AUB	ET-10mm	Simple hyperplasia

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
110	Mrs.Pongodi	43	1110/14	0412140008	P2	+					AUB	ET-5mm	Proliferative pattern
111	Mrs.Sathyabama	48	1111/14	0412140014	P3	+					AUB	ET-8mm	Proliferative pattern
112	Mrs.Munniyammal	54	1114/14	2811140050	P3					+	AUB	ET-5mm	Atrophic endometrium
113	Mrs.Shakila	44	1140/14	11121400005	P2	+					AUB	ET-17mm	Simple hyperplasia
114	Mrs.Selvi	32	1143/14	1212140018	P2	+					AUB	ET-10mm	Proliferative pattern
115	Mrs.Elavarasi	50	1145/14	1212140008	P3		+				AUB	ET-15mm	Complex hyperplasia
116	Mrs.Rani	45	1169/14	1612140018	P2			+			AUB	ET-7mm	Atrophic endometrium
117	Mrs.Puspha	44	1184/14	1812140044	P2	+					AUB	ET-polyp	Endometrial polyp
118	Mrs.Murugammal	45	1188/14	1312140012	P2	+					AUB	ET-8mm	Menstrual phase
119	Mrs.Shanthi	38	1199/14	1312140018	P2	+					AUB	ET-12mm	Disordered proliferative endometrium
120	Mrs.Kanagavalli	40	1202/14	2612140001	P3	+					AUB	ET-10mm	Secretory pattern
121	Mrs.Chellammal	65	022/15	2212140008	P4					+	AUB	ET-17mm	Atypical hyperplasia
122	Mrs.Kamatchi	33	026/15	0601150014	P2		+				AUB	ET-15mm	Simple hyperplasia
123	Mrs.Mannikam	48	044/15	2201150005	P3	+					AUB	ET-12mm	Endometrial metaplasia
124	Mrs.Akshiliya	50	083/15	2601150004	P3		+				AUB	ET-11mm	Proliferative pattern
125	Mrs.Rathi	46	097/15	2901150046	P2	+					AUB	ET-10mm	Proliferative pattern
126	Mrs.Sundari	30	103/15	3101150002	P2	+					AUB	ET-12mm	Secretory pattern
127	Mrs.Lalitha	45	112/15	0302150005	P2	+					AUB	ET-15mm	Proliferative pattern
128	Mrs.Jaclin	37	113/15	0302150002	P2		+				AUB	ET-10mm	Secretory pattern

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
129	Mrs.Thayar	35	114/15	0302150008	P2	+					AUB	ET-12mm	Proliferative pattern
130	Mrs.Shanthi	40	117/15	2901150048	P2		+				AUB	ET-18mm	Complex hyperplasia
131	Mrs.Patchyammal	45	118/15	0402150010	P2			+			AUB	ET-6mm	Proliferative pattern
132	Mrs.Vasuki M	41	120/15	0402150009	P3	+					AUB	ET-10mm	Proliferative pattern
133	Mrs.Selvi	42	133/15	0902150022	P3			+			AUB	ET-6mm	Hormonal changes
134	Mrs.Malar	40	138/15	1002150053	P2			+			AUB	ET-10mm	Menstrual phase
135	Mrs.Lakshmi	48	139/15	05021500109	P2	+					AUB	ET-8mm	Secretory pattern
136	Mrs.Kavitha	35	155/15	1602150017	P1	+					AUB	ET-10mm	Proliferative pattern
137	Mrs.Kalavathy	46	187/15	1702150039	P2		+				AUB	ET-12mm	Simple hyperplasia
138	Mrs.Malliga	44	188/15	2602150039	P2	+					AUB	ET-15mm	Secretory pattern
139	Mrs.Vijaya	40	195/15	2702150002	P2			+			AUB	ET-10mm	Simple hyperplasia
140	Mrs.Kannagi	29	216/15	0403150004	P1	+					AUB	ET-8mm	Simple hyperplasia
141	Mrs.Vijaya	45	231/15	1103150015	P2	+					AUB	ET-10mm	Disordered proliferative endometrium
142	Mrs.Vijayalakshmi	40	241/15	0903150053	P2		+				AUB	ET-8mm	Secretory pattern
143	Mrs.Mohana	34	255/15	1103150013	P1		+				AUB	ET-10mm	Proliferative pattern
144	Mrs.Jayanthi	35	322/15	2503150020	P1	+					AUB	ET-11mm	Simple hyperplasia
145	Mrs.Lakshmi	47	428/15	1604150042	P2		+				AUB	ET-8mm	Endometrial adenocarcinoma
146	Mrs. Sathya	40	443/15	2104150029	P1	+					AUB	ET-7mm	Secretory pattern
147	Mrs.Kanammal	39	457/15	2404150045	P2	+					AUB	ET-10mm	Simple hyperplasia

S.№	NAME	AGE	HISTOPATHOLOGY №	I.P.№	PARITY	CLINICAL FEATURES					CLINICAL DIAGNOSIS	USG FINDINGS	HISTOPATHOLOGICAL DIAGNOSIS
						MR	MTR	MMTR	PMR	PMB			
148	Mrs.Chellamal	55	458/15	1504150017	P2					+	AUB	ET-4mm	Atrophic endometrium
149	Mrs.Rani	58	459/15	1604150031	P3					+	AUB	ET-4mm	Atrophic endometrium
150	Mrs.Malar	42	467/15	2002150075	P2	+					AUB	ET-7mm	Disordered proliferative endometrium

ER AND PR STATUS OF ENDOMETRIUM IN NON-MALIGNANT AND MALIGNANT ENDOMETRIUM

S.№	NAME	AGE	HISTOPATHOLOGY №	HISTOPATHOLOGICAL DIAGNOSIS	ER (PP %)	PR (PP %)
1	Mrs.Padmavathy	45	641/13	Proliferative pattern	90	98
2	Mrs Mohana Tirunavukarasu	48	659/13	Complex hyperplasia	0	0
3	Mrs.Lakshmi	45	726/13	Simple hyperplasia	70	79
4	Mrs.Pushnavathi	43	796/13	Atypical hyperplasia	54	53
5	Mrs.Chellammal	49	102/14	Proliferative pattern	82	97
6	Mrs.Amishiya	45	107/14	Simple hyperplasia	65	68
7	Mrs.Selvi	50	213/14	Simple hyperplasia	60	53
8	Mrs.Kasthuri	43	285/14	Simple hyperplasia	63	63
9	Mrs.Kanniga	42	314/14	Complex hyperplasia	60	62
10	Mrs.Lakshmi	49	323/14	Endometrial adenocarcinoma	29	27
11	Mrs.Sagunthala	45	388/14	Complex hyperplasia	55	60
12	Mrs.Radha	50	392/14	Complex hyperplasia	0	65
13	Mrs.Sellamallal	50	416/14	Simple hyperplasia	0	0
14	Mrs.Kanchana	44	419/14	Complex hyperplasia	59	57
15	Mrs.Eganthal	45	429/14	Proliferative pattern	96	89
16	Mrs.Saraswathy	48	545/14	Simple hyperplasia	48	60
17	Mrs.Vedhavalli	49	550/14	Complex hyperplasia	59	63

S.№	NAME	AGE	HISTOPATHOLOGY №	HISTOPATHOLOGICAL DIAGNOSIS	ER (PP %)	PR (PP %)
18	Mrs.Alamelu	49	683/14	Proliferative pattern	97	99
19	Mrs.Chellamal	50	708/14	Simple hyperplasia	59	67
20	Mrs.Shanthi	47	736/14	Simple hyperplasia	0	0
21	Mrs.Renuga	46	753/14	Proliferative pattern	88	92
22	Mrs.Lalitha	48	791/14	Atypical hyperplasia	49	53
23	Mrs.Ellammal	45	822/14	Proliferative pattern	85	89
24	Mrs.Kuppu	46	849/14	Complex hyperplasia	60	63
25	Mrs.Lakshmi	44	893/14	Proliferative pattern	98	95
26	Mrs.Vijaya	44	947/14	Proliferative pattern	93	0
27	Mrs.Kanniyammal	50	979/14	Proliferative pattern	0	0
28	Mrs.Alamelu	45	1018/14	Proliferative pattern	89	94
29	Mrs.Malliga	50	1024/14	Simple hyperplasia	68	
30	Mrs.Pushpavathy	41	1036/14	Simple hyperplasia	59	78
31	Mrs.Pongodi	43	1110/14	Proliferative pattern	84	98
32	Mrs.Sathyabama	48	1111/14	Proliferative pattern	94	92
33	Mrs.Shakila	44	1140/14	Simple hyperplasia	59	68
34	Mrs.Elavarasi	50	1145/14	Complex hyperplasia	57	55
35	Mrs.Akshiliya	50	083/15	Proliferative pattern	97	91
36	Mrs.Rathi	46	097/15	Proliferative pattern	0	0
37	Mrs.Lalitha	45	112/15	Proliferative pattern	0	0

S.№	NAME	AGE	HISTOPATHOLOGY №	HISTOPATHOLOGICAL DIAGNOSIS	ER (PP %)	PR (PP %)
38	Mrs.Patchyammal	45	118/15	Proliferative pattern	98	96
39	Mrs.Vasuki M	41	120/15	Proliferative pattern	92	97
40	Mrs.Kalavathy	46	187/15	Simple hyperplasia	51	52
41	Mrs.Lakshmi	47	428/15	Endometrial adenocarcinoma	26	0

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